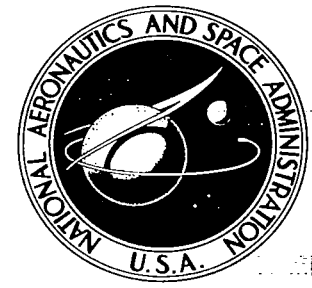
NASA
EBR-
pt.2
c.1

NASA CR-172

NASA CONTRACTOR REPORT



NASA CR-172

COPY: RE
AFWL (WL
KIRTLAND AFB

0062878

TECH LIBRARY KAFB, NM

THE EFFECT OF BEDREST ON VARIOUS PARAMETERS OF PHYSIOLOGICAL FUNCTION

PART II. EXPERIMENTAL DESIGN

by C. Vallbona, F. B. Vogt, D. Cardus, and W. A. Spencer

Prepared under Contract No. NAS 9-1461 *by*
TEXAS INSTITUTE FOR REHABILITATION AND RESEARCH
Houston, Texas
for

NATIONAL AERONAUTICS AND SPACE ADMINISTRATION • WASHINGTON, D. C. • MARCH 1965

NASA CR-172

TECH LIBRARY KAFB, NM
0062878

THE EFFECT OF BEDREST ON VARIOUS PARAMETERS OF PHYSIOLOGICAL FUNCTION

PART II. EXPERIMENTAL DESIGN

By C. Vallbona, F. B. Vogt, D. Cardus, and W. A. Spencer

Distribution of this report is provided in the interest of information exchange. Responsibility for the contents resides in the author or organization that prepared it.

Prepared under Contract No. NAS 9-1461 by
TEXAS INSTITUTE FOR REHABILITATION AND RESEARCH
Houston, Texas

for

NATIONAL AERONAUTICS AND SPACE ADMINISTRATION

For sale by the Office of Technical Services, Department of Commerce,
Washington, D.C. 20230 -- Price $4.00

THE EFFECT OF BEDREST ON VARIOUS PARAMETERS OF PHYSIOLOGICAL FUNCTION

PART II. EXPERIMENTAL DESIGN

By C. Vallbona, M.D., F. B. Vogt, M.D., D. Cardus, M.D., and W. A. Spencer, M.D.

ABSTRACT

An Immobilization Study Unit was organized at the Texas Institute for Rehabilitation and Research under contract with the Manned Spacecraft Center of NASA to study the consequences of immobilization and its mechanisms. During 1963, a pilot experiment and two studies aimed at: a) quantifying cardiovascular deconditioning resulting from 3 days and 14 days of bedrest, b) investigating the mechanisms of orthostatic hypotension, c) evaluating indirect techniques of measurement of the cardiac cycle and its phases, d) measuring bone demineralization, and e) evaluating the effect of isometric exercises during bedrest in preventing deconditioning and demineralization. This report describes the study, the subjects, and the experimental conditions. The Appendix includes a master protocol and descriptions of techniques.

FOREWORD

This study is a part of a NASA investigation of the effect of bedrest on various parameters of physiological function. It was sponsored by NASA Manned Spacecraft Center under Contract NAS-9-1461, with Dr. Lawrence F. Dietlein, Chief, Space Medicine Branch serving as Technical Monitor.

This study was conducted in the Immobilization Study Unit of the Texas Institute for Rehabilitation and Research, The Texas Medical Center. The authors are affiliated with Baylor University College of Medicine as follows: Dr. Vallbona, Departments of Rehabilitation, Physiology, and Pediatrics; Dr. Vogt, Department of Rehabilitation; Dr. Cardus, Departments of Rehabilitation and Physiology, and Dr. Spencer, Department of Rehabilitation.

The authors express their appreciation to the numerous investigators and research assistants who participated actively in the preparation and execution of the experiment. The assistance of Professor Dr. H. E. Hoff, Professor Dr. E. S. Wallis, Doctors T. B. Watt, C. B. Breckenridge, G. M. Harrison, R. E. Carter, C. R. Peterson, E. N. Zuniga, B. Sher, J. E. Kirkham, W. C. Beasley, and Mrs. M. Mitchell is especially acknowledged. Mrs. D. Bellis gave invaluable assistance in her role as coordinator of the project; Miss M. Walters was most helpful in providing dietary supervision as well as in preparing the report; and Mrs. S. Gotcher contributed helpful editorial assistance. The cooperation received from the Crew Systems Division, Space Medicine Branch, Bioinstrumentation Section, Experimental Medicine Section, Data Systems Development Branch, and Flight Systems Branch of the Manned Spacecraft Center of NASA made possible the successful completion of the studies within the expected time. The subjects who volunteered for the studies deserved recognition for their willingness and enthusiasm.

TABLE OF CONTENTS

THE EFFECT OF BEDREST ON VARIOUS PARAMETERS OF PHYSIOLOGICAL FUNCTION

PART II. EXPERIMENTAL DESIGN

By C. Vallbona, M.D., F. B. Vogt, M.D., D. Cardus, M.D., and W. A. Spencer, M.D.

SUMMARY

There is need to delineate the physiological effects of weightlessness in order to anticipate and prevent deleterious effects of space flights. To some extent bedrest in the horizontal position simulates the conditions of weightlessness. In spite of existing knowledge on the effects of prolonged bedrest, there is need to study further some of the consequences of immobilization and their mechanisms.

The Texas Institute for Rehabilitation and Research under contract with the Manned Spacecraft Center of NASA organized an Immobilization Study Unit. During 1963, a pilot experiment and two studies were conducted in order to: a) quantitate the degree of cardiovascular deconditioning resulting from 3 days and 14 days of bedrest, b) investigate the mechanisms of orthostatic hypotension, c) evaluate the information provided by indirect techniques of measurement of the cardiac cycle and its phases, d) measure the degree of bone demineralization, and e) evaluate the possible effect of isometric exercises during bedrest in preventing cardiovascular deconditioning and bone demineralization. This report gives a detailed description of the plan of study, the subjects selected, and the experimental conditions of the studies. The Appendix includes a detailed master protocol and descriptions of the techniques and procedures. The results of the studies are presented and discussed in separate reports.

INTRODUCTION

There are numerous scientific reports on the physiological effects of bedrest, but as pointed out previously [1] much of the current knowledge on this subject derives from studies carried out under various experimental conditions in relatively few and small groups of subjects of different age, physique, and physiological conditions.

A renewal of the interest in the physiological effects of immobility came about in anticipation of manned space flights because of theoretical considerations of the possible physiological effects of weightlessness. [2,3] Clinical observations following some of the first manned space flights confirmed the impression that prolonged weightlessness could create physiological problems of undetermined severity. [4,5] Outstanding among these problems is orthostatic hypotension. In an attempt to understand the mechanisms of physiological deconditioning produced by weightlessness, it has been necessary to set up experiments on the ground under conditions somewhat analogous, but not identical, to those obtained in an environment of zero gravity. Weightlessness can be achieved only in orbital or space flights or in the brief duration of Keplerian trajectories of high speed aircraft. Experimental conditions resembling most closely those of zero gravity are prolonged bedrest and prolonged immersion in water. Prolonged bedrest, if maintained rigorously in the horizontal position, allows the cardiovascular system to function without significant influence of gravitational forces. Bedrest, however, does not produce sensory deprivation and does not eliminate the effect of muscular activity which can be considerable when the body is not kept in a fixed position. This is difficult to achieve, for even the use of casts does not prevent motion of the joints. [6] Immersion in water is advantageous for it utilizes the buoyancy of the water to counteract the effect of gravity regardless of the degree of mobility; therefore, it may simulate more closely the conditions of space flight, but the hydrodynamic forces acting on the soft tissues create cardiovascular conditions that are not present in weightlessness.

In an attempt to delineate further the physiological effects of bedrest, especially those on the cardiovascular system, the Texas Institute for Rehabilitation and Research under a contract with the Manned Spacecraft Center of NASA organized an Immobilization Study Unit.

PURPOSE

To fulfill the requirements of the contract, the staff of the Immobilization Study Unit, in agreement with the technical monitor of NASA, established the following objectives:

1. Quantitate the degree of cardiovascular deconditioning resulting from bedrest of variable duration.

2. Investigate the mechanisms of orthostatic hypotension resulting from bedrest.

3. Evaluate the information provided by indirect techniques of measurement of the cardiac cycle and its phases.

4. Measure the degree of bone demineralization that occurs during bedrest.

5. Evaluate the effect of isometric exercises during bedrest in preventing cardiovascular deconditioning and bone demineralization.

In addition, the study should provide opportunity for the following:

1. To adapt a bone densitometry X-ray technique to quantitate bone demineraliztion. This aspect of the study would be directed by the investigators of the Nelda Childers Laboratory of Human Nutrition Research of Texas Woman's University.

2. To test the practicality of a system for bedside physiological monitoring of subjects during bedrest.

3. To set up a system for data processing and development of computer techniques for analyzing cardiovascular data.

Successful accomplishment of these objectives required the coordination of efforts of various groups of investigators. The following groups participated in the studies: Departments of Rehabilitation, Physiology, Pediatrics, Radiology, Medicine, and the Biomathematics Research Laboratory of Baylor University College of Medicine; The Nelda Childers Laboratory for Human Nutrition Research of Texas Woman's University; The Endocrine-Biochemistry Laboratory of the University of Utah; The Crew Systems Division, Space Medicine Branch, the Bio-Instrumentation Section, the Experimental Medicine Section, the Data Systems Development Branch, and the Flight Systems Branch of the Manned Spacecraft Center of NASA.

The design of the experiments was prepared by the investigators of the Texas Institute for Rehabilitation and Research in cooperation with personnel of the NASA Space Medicine Branch, Crew Systems Division. Numerous consultants from the different groups indicated previously participated in the discussion of the experimental design and took an active part in the conferences at which progress reports of the studies were given.

PLAN

During the year of 1963, a pilot experiment and two studies were conducted. Study I was aimed at evaluating the physiological effects of short-term bedrest (3 days).

This study included two separate periods. In the first period six subjects were in bedrest for three days and in the second period the same subjects performed isometric exercises during three days of bedrest. Study II was carried out to evaluate the effect of more prolonged bedrest (14 days). A new group of six subjects participated in a first period of fourteen days of bedrest. Five of the same group and an additional subject took part in a second period of fourteen days of bedrest with isometric exercise. Each period of each study was preceded and followed by days of observation. At the onset and at the end of each period of bedrest the subjects were submitted to a passive tilt test. The schedule of these studies is shown in Figure 1.

In the month of March, 1963, a pilot experiment was conducted to evaluate the safety and feasibility of the use of the Flack maneuver to prevent cardiovascular deconditioning occurring in bedrest. Six subjects participated in a first period of three days of bedrest preceded and followed by one day of observation. Five of these subjects participated also in the second period of three days of bedrest during which the individuals were required to perform a Flack maneuver for a duration of about 15 seconds every 30 minutes during the 6:00 a.m. to 12:00 midnight period. The results of this study are presented in a separate report. [7]

SUBJECTS

Healthy adults volunteered to take part as subjects of these studies. They were recruited from colleges and universities of the Houston metropolitan area and from employment agencies. Each subject received a stipend for his participation.

A total of 35 individuals indicated a desire to participate. Twenty-eight of these were interviewed individually and filled out a special questionnaire designed to facilitate the medical screening. At the end of the interview, each subject underwent a physical examination and an electrocardiogram was obtained. In addition, each individual selected for the study was submitted to a psychiatric interview and to a sociological interview.

Six subjects participated in Period 1 and Period 2 of Study I. Their physical characteristics are indicated in Table 1. The following is a summary of medical information pertaining to them:

1. R. K. W. (TIRR # 70001) was a 27 year old newswriter. His past history and review of systems were not remarkable. The physical examination revealed an apparently healthy individual with a slightly flabby appearance but with normal proportion of trunk measurements and extremities. He wore glasses all the time. The psychiatric evaluation indicated that the subject appeared somewhat passive, dependent, and exhibited feelings of inadequacy. However, it was believed he would adjust to the demands of the study without difficulty.

STUDY I

S	M	T	W	T	F	S
MAY			1	2	3	4
5	6	7	8	9	10	11
12	13	14	15	16	17	18
19	20	21	22	23	24	25

STUDY II

S	M	T	W	T	F	S
JULY	15	16	17	18	19	20
21	22	23	24	25	26	27
28	29	30	31	AUG. 1	2	3
4	5	6	7	8	9	10
11	12	13	14	15	16	17
18	19	20	21	22	23	24
25	26	27	28	29	30	31
SEPT. 1	2	3	4	5	6	7

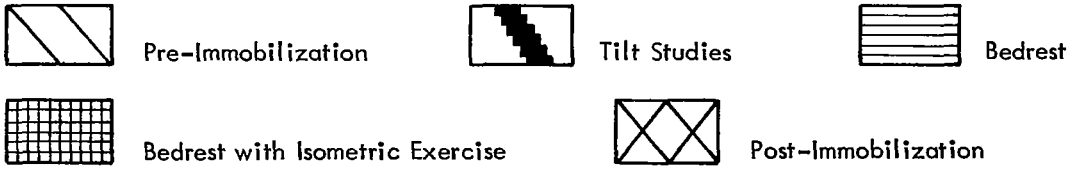


Figure 1. Schedule of Study I and Study II.

TABLE 1

SUBJECTS PARTICIPATING IN STUDY I
TWO PERIODS OF THREE DAYS OF BEDREST

TIRR Subject No.	Name	Age (years)	Height (centimeters)	Weight (kilograms)	Body Surface Area (m^2)	Usual Occupation
70-0-01	RKW	27	183.0	81.8	2.04	Newswriter
70-0-06	CBB	39	177.8	75.0	1.92	Oil refinery process operator (on strike)
70-0-07	RNM	21	177.8	72.7	1.90	Clerk
70-0-08	WRS	21	190.5	75.0	2.02	Student
70-0-09	THL	37	180.4	78.1	1.98	Oil refinery process operator (on strike)
70-0-10	RGW	40	175.2	76.8	1.92	Oil refinery process operator (on strike)

SUBJECTS PARTICIPATING IN STUDY II
TWO PERIODS OF FOURTEEN DAYS OF BEDREST

70-0-11	ACL	33	170.3	62.7	1.73	Student athlete
70-0-12	TGO*	21	188.0	79.2	2.06	Student
70-0-13	MGO	24	177.8	79.2	1.97	Student athlete
70-0-14	DC	24	180.4	75.0	1.94	Student
70-0-16	CLB**	24	185.5	85.7	2.10	Student counselor
70-0-17	CP	34	180.4	77.0	1.97	School teacher
70-0-18	ACI***	22	165.0	50.0	1.54	Student athlete

* Participated in first period only (fourteen days of bedrest)
** Had to be dismissed on the thirteenth day of bedrest of the second period
*** Participated in second period only (fourteen days of bedrest with isometric exercise)

2. R. G. W. (TIRR # 70010) was a 40 year old process operator (on strike) for an oil refinery. His past history and review of systems were not remarkable. The physical examination revealed a moderately flabby individual with a slightly protrudent abdomen and a moderate amount of fat in the subcutaneous tissues. The physical examination revealed no pathological findings. A psychiatric evaluation indicated he was outgoing and extroverted. He did not exhibit anxiety and seemed to enjoy the challenge of the study. It was believed he might provide the humor for the group and no problems were anticipated.

3. T. H. L. (TIRR # 70009) was a 37 year old process operator (on strike) for an oil refinery. His past history and review of systems were not remarkable. Physical examination revealed the proportions of measurements of trunk and extremities to be within normal limits. There were no pathological findings. Psychiatric evaluation indicated that the subject had some emotional instability in his past but recently had shown more maturity. No problem was anticipated with respect to his participation in the study.

4. C. B. B. (TIRR # 70006) was a 39 year old process operator (on strike) for an oil refinery. Past history revealed he had had pneumonia and otitis media several years before the interview. The review of systems was not remarkable. Physical examination revealed a well-proportioned individual with normal body proportions, very slight protrudence of the abdomen and slight increase of fat in subcutaneous tissue. There were no pathological findings. The psychiatric evaluation indicated this subject was well adjusted in all walks of life and was able to cope satisfactorily with all stresses that confronted him. His emotional response was somewhat shallow, and no difficulty was anticipated with respect to his participation in the study.

5. W. R. S. (TIRR # 70008) was a 21 year old college student who was employed by his father. The past history and review of systems were not remarkable and the subject denied any symptoms of postural intolerance at any time. (This was pertinent since the subject exhibited orthostatic hypotension in the passive tilt test before bedrest.) Physical examination revealed a tall individual somewhat asthenic. The subject wore contact lenses. The psychiatric evaluation indicated that he was an overly dependent individual, and it was believed that he might be somewhat demanding or exhibit some anxiety during the course of the study. However, it was believed he could complete the study satisfactorily.

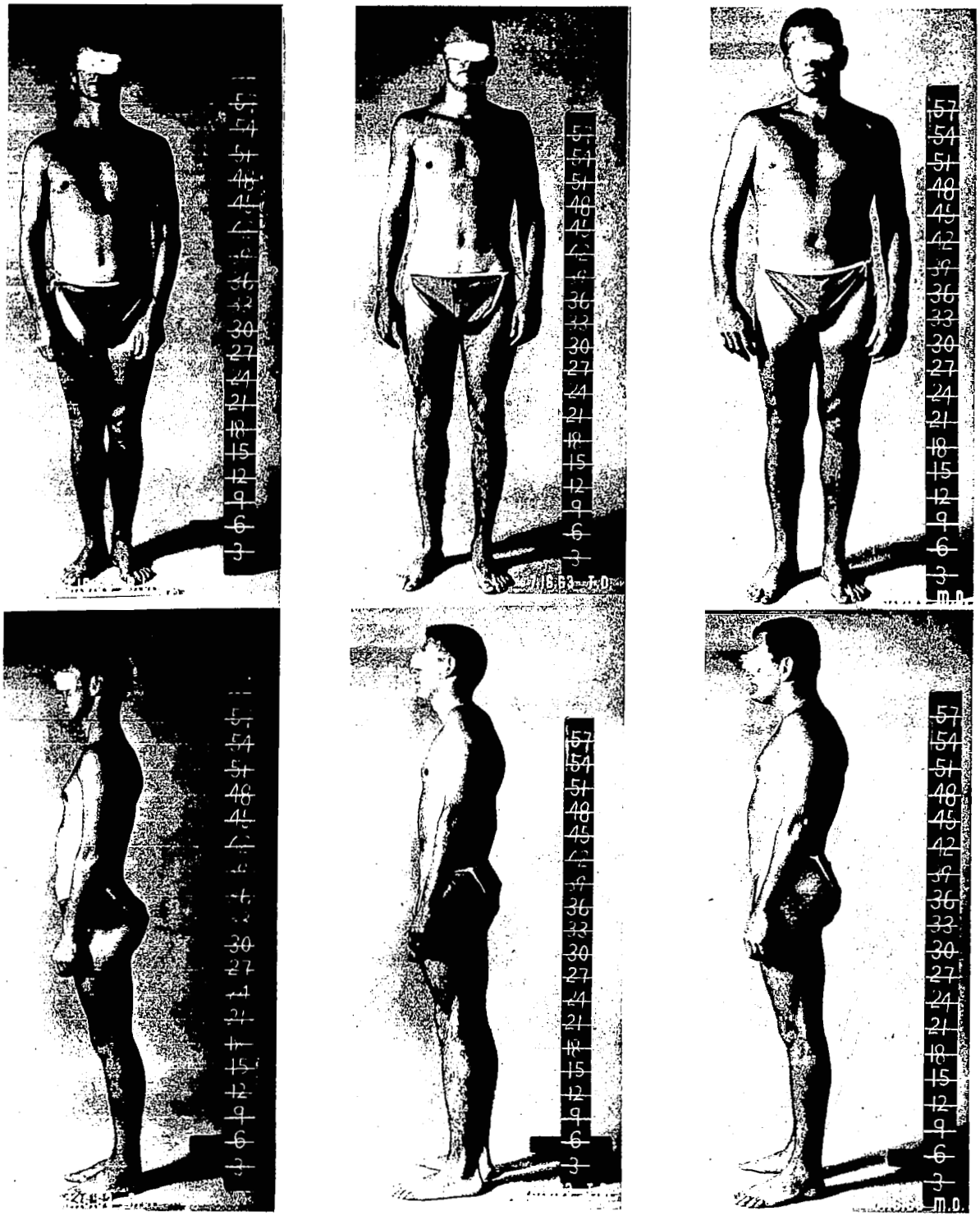
6. R. N. McA. (TIRR # 70007) was a 21 year old clerk working part-time in a federal office. He was considered to be in good health at the time of the study although past history revealed that he had Reiter's Syndrome with the onset in February, 1962. He was treated with Cortisone for several weeks and the symptoms cleared. In the fall of 1962, he had a very mild relapse of the syndrome but after two weeks of treatment the symptoms cleared. For at least four months prior to the study, the patient had not received steroids. The review of systems was within normal limits except for occasional discharge of the urethra. The physical examination revealed an apparently healthy individual with normal body proportion and good development of the muscle groups. A psychiatric evaluation indicated that this subject was introverted but well integrated. His history showed some schizoid tendencies, but it was believed he would accept the conditions of the study in a stoic manner.

The sociological evaluation of these subjects revealed the three oldest men came from rather limited backgrounds without college education. The three youngest men had attended college. Four subjects were enthusiastic waterskiers and two had flying experience, either as licensed pilot or student flyer. Economic considerations were the primary motives for participation in the study. At the interview after the experiments all subjects complained of excessive laboratory tests that required numerous venous punctures. Only one complained of boredom. All were unanimous in their positive statements regarding group congeniality and consideration shown to the subjects by the personnel of the project. Three of the subjects stated that they would not repeat this experience under any circumstances; three would be willing to do so if necessary. One of the individuals was critical of the orderlies who did not show sufficient orientation in regard to basic schedules and routines.

A total of seven subjects participated in Study II. Five of them stayed for the two periods. Subject T. G. O. participated in the first period only and Subject A. C. I. took part in the second period only. Subject C. L. B. had to be dismissed at the end of the thirteenth day of bedrest with isometric exercises due to a sudden medical emergency of his brother. The subject, however, did return for follow-up studies five days after dismissal.

The physical characteristics of the subjects who participated in Study II are shown in Table 1. Photographs showing the physical appearance of these subjects are presented in Figure 2. A detailed description of each of these seven subjects is as follows:

1. A. C. L. (TIRR # 70011) a 33 year old university student and middle distance track runner was considered to be in good health. Both his Achilles tendons had been injured in a sporting accident

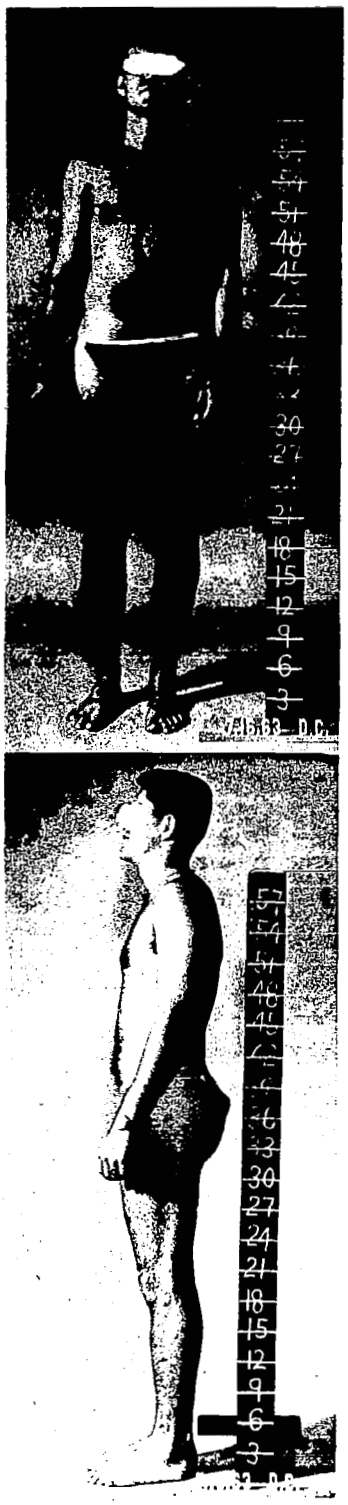


TIRR # 70-0-11 A. L.

TIRR # 70-0-12 T. O.

TIRR # 70-0-13 M. O.

Figure 2. Photographs of subjects who participated in Study II.

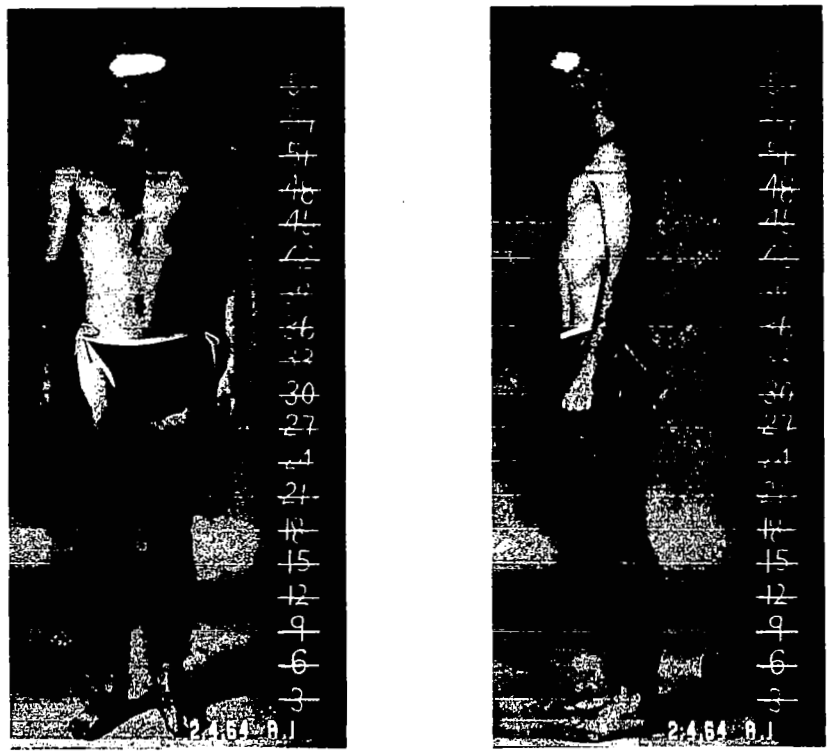


TIRR # 70-0-14 D. C.

TIRR # 70-0-16 C. B.

TIRR # 70-0-17 C. P.

Figure 2. (continued)



TIRR # 70-0 18 A. I.

Figure 2. (concluded)

in December, 1961, requiring surgical repair. This was considered irrelevant to the study. The review of systems was not remarkable. Physical examination revealed a well-developed adult male with normal amount of muscle mass. He had a marked sinus arrhythmia and a low pulse rate of 50 per minute. On psychiatric evaluation he appeared a quiet, self-contained person. He seemed to make stable interpersonal relationships and to get along well with other people. He was strongly motivated to complete the project because of his financial needs. There was no evidence of anxiety or other emotional disturbances. It was anticipated that he would tolerate the experience quite well. Upon dismissal after the first period of bedrest, the subject stated he had some soreness in the Achilles tendon on both sides and a bit of tightness in his chest. Also he had a lymphangitis of the dorsum of the right hand as a result of a needle puncture on August 5, 1963. With Terramycin therapy the symptoms subsided in 24 hours. He participated in the second period of bedrest with isometric exercises without difficulty.

2. T. G. O. (TIRR # 70012) a 22 year old college student was considered to be in good health. His past history and review of systems were not remarkable. The physical examination revealed an apparently healthy, well-developed individual with normal muscle build. During the psychiatric interview, the subject was cooperative and friendly, appeared highly intelligent, and stated he was valedictorian of his high school class. He had been active in sports, but also enjoyed sedentary activities such as reading. It was thought that he would get along well with other people and would be very cooperative. His motivation came from a desire to be a participant in the space program. There was no evidence of emotional disorder. His physical condition at the time of discharge was considered to be the same as that prior to admission for the study. He did not participate in the second period of bedrest with isometric exercises.

3. M. G. O. (TIRR # 70013) a 24 year old university student and athlete was considered to be in good health and there were no contraindications to admission for the study. His past history and review of systems were not remarkable. The physical examination revealed an apparently healthy, well-developed, well-nourished individual with a normal muscular build. The psychiatric evaluation noted that he tended to have periods of restlessness at times. He appeared to be an outgoing, open, and stable person. He seemed dedicated to his work and it was felt that he would get along quite well with the group. It was thought that he would have no difficulty in completing the project, although he might become restless as a result of immo-

bility. This subject developed orthostatic hypotension after immobilization. He complained of being tired for the first two days after bedrest with some soreness of muscles especially the extensors of the left forearm. There was slightly more protuberance of the abdominal wall than before bedrest, but the muscle strength was normal as it was before bedrest. He participated in the second period without difficulty.

4. D. C. III (TIRR # 70014) a 25 year old university student was considered in good health with no contraindications to admission for the study. The subject gave a history of food poisoning at age sixteen with complete recovery. The physical examination revealed a well-developed adult male with normal amount of muscle mass. There was a small, well-healed scar on the anterior surface of the leg from a fracture which occurred ten years previous. On psychiatric evaluation he appeared intelligent and stated that he had volunteered for the experiment for financial reasons. He tended to get impatient with things that were not precise, clear cut, and scientific. He was compulsive and interested in research; it was thought that these factors would work for his successful completion of the project. The interviewer felt that the subject probably would want explanations as to reasons behind various procedures to be carried out. The subject developed orthostatic hypotension after immobilization. He had marked tenderness in his heels and noticeable protuberance of the abdominal wall following the first bedrest period. He noticed that he was more tired than usual after moderate activity. He participated in the second period of bedrest without difficulty.

5. C. L. B. (TIRR # 70016) a 26 year old college student was considered in good health and there were no contraindications to admission for the study. His past history and review of systems were non-contributory. The physical examination revealed a well-developed, well-nourished adult male who was somewhat flabby with less preponderance of muscle mass than the other subjects. The psychiatric evaluation reported that he was intelligent and an extrovert person who appeared flippant and carefree. He had been successful in his scholastic career and it was felt that he would probably take things more seriously than his attitude might indicate and because of his pride in his adaptability, he should see the project through. There was no anxiety or evidence of any emotional illness. The interviewer felt that his flippant attitude might at times cause some friction with other members of the group, but it was felt that if this happened he would probably conform to group pressure in order to prevent social ostracism. This subject developed orthostatic hypotension following immobilization. Following bedrest, there was swelling of the dorsum of the right hand which was due to lymphangitis

and later thrombophlebitis of the superficial vein of the dorsum of the hand due to needle puncture during tilt on August 5, 1963. He was treated with Terramycin. The subject stated that he felt dizzy and tired for two days after the bedrest period after which time these symptoms were not noticeable. He participated in the second period, but had to be dismissed after the thirteenth day to go home because his brother was in a car accident. He developed orthostatic hypotension in the passive tilt test before dismissal. He returned for follow-up studies.

6. C. P. (TIRR # 70017) a 35 year old school teacher was considered to be in good health and there were no contraindications to admission for the study. Physical examination revealed a well-developed adult male with normal amount of muscle mass. There was a laparotomy scar at the right lower quadrant. There was a fine linear scar in the right eyebrow and a scar on the thumb on the right hand which were the result of an auto accident while the subject was in the service in Japan in 1951. The thumb had a permanent contracture in flexion and inward rotation. The subject wore glasses for farsightedness. The psychiatric evaluation revealed an extrovertive person who liked people and was friendly and cooperative during the interview. His primary interests were outdoor sports and reading. His reason for volunteering for this project was his interest in contributing to the space program. There was no evidence of anxiety, depression, or other emotional problems. He appeared a stable person who would do well in the project. This subject did not have orthostatic hypotension at the end of the first period of bedrest, but it occurred after the second period of bedrest.

7. A. C. I. (TIRR # 70018) a 22 year old college student and athlete was considered to be in good health. There were no contraindications to his admission for the second period of the study to replace Subject T. G. O. The physical examination revealed a short but well-developed adult male with good proportions for his physical dimensions. There was a preponderance of muscle bulk in all muscle groups. No formal psychiatric evaluation interview was conducted, but he appeared intelligent and extrovertive, with a good sense of humor. He was tense on the day of the tilt tests before the second period of bedrest and he developed orthostatic hypotension on a first tilt trial, but after reassurance he withstood a second tilt without difficulties. The passive tilt after bedrest with exercise was well tolerated.

The sociological evaluation reported that six of the seven subjects had been enrolled in college just prior to participation in the study. The seventh had received his Bachelor's degree and was a teacher at the time of the study. All subjects were

attending college and had some type of supplementary financial aid such as scholarship, grant-in-aid, and fellowship. In addition, the majority usually had part-time employment during the academic year. The subjects indicated that under usual circumstances they were quite active from a physical standpoint and carried out a great deal of physical activity especially those engaged in sports. Each subject frankly admitted that finances had been his primary motivation for participation in the study, and with only one exception the subjects entered into this experience with a positive, constructive attitude toward their individual roles in the study and toward the cohesiveness of the group. The group morale was good and interpersonal relationships remained at a high level throughout the first period of the second study, upon return from leave of absence, and at the beginning of the second period. The major negative comments were in respect to the large quantity of food, lack of privacy (which later was remedied by putting up curtains around each subject's bed), using the bedpan in a supine position, the noise, and inefficient orderlies. There was no great amount of feeling expressed in respect to these criticisms. There was a remarkable drop in the morale of the group by the middle of the second period and the subjects complained bitterly of the freeze-dried food diet they were being served at that time. In a group session held by the subjects and the social worker, the subjects were vocal and voluble in respect to their assessment of the quality of the food. Some subjects complained of the loss of independence and having to ask others to do things for them.

EXPERIMENTAL CONDITIONS

A. Bedrest

Throughout the first period of Study I and of Study II each subject remained in bedrest in the horizontal position. At least one attendant was present in the Immobilization Study Unit at all times to observe the individuals and to be sure that they maintained adequate position. A physician was in the ward or in the adjacent areas at all times. During the daytime hours other personnel directly involved with the investigation were present in addition to the attendants, and this contributed to the reinforcement of the bedrest conditions. The subjects were allowed to move freely in bed maintaining the horizontal position and they were allowed one pillow. Emunctory functions were performed on a bedpan in the horizontal position. Changes of linen and bathing were done by male attendants every day while retaining the subjects in the lying down posture. These allowances resulted in some movement of the arms above the level of the bed, but the trunk and the legs remained on the same plane. The subjects accepted the restrictions, but they had an unconscious tendency in the first hours of bedrest to elevate the knees or to raise the trunk above the bed level. The constant observation of the subjects resulted in their rapid training in becoming aware of these transgressions. In general, the investigators were satisfied that bedrest was observed as stipulated.

B. Observation before and after bedrest

In the days preceding and following each period of bedrest or bedrest with isometric exercises the subjects remained hospitalized but they could be up and about. They could leave the hospital for short periods provided they did not drink or eat anything. All of their meals of the special diet which were eaten in the hospital were of known composition. In addition to the liquids served with meals, the subjects could drink as much distilled water as they wanted. The intake and output were carefully measured and recorded. The excreta were saved for analysis.

C. Environment

The Immobilization Study Unit of the Texas Institute for Rehabilitation and Research is located in the basement of the building. It is fully air-conditioned. The temperature and humidity were maintained fairly constant at 75° F and 70% respectively throughout the studies. There were no measurements made of these conditions on a routine basis.

The lighting is provided by fluorescent lamps with a light intensity of approximately 55 foot candles. Each subject had a lamp at the head of his bed to provide him with better luminosity for reading. The lights were turned off every night at 9:00 p.m. and turned on at 7:00 a.m. During the dark hours there was a minimum of light around the monitoring instruments and at the table of the attendant to allow him to write his observations. There was a television set in the room which was turned off every night at 11:00 p.m.

There was a great deal of activity and noise in the room in the daytime hours throughout the two studies due to the constant movement of personnel carrying out numerous laboratory and physiological measurements.

D. Diets

The meals given to the subjects were planned and prepared by a graduate research dietitian and were of known composition. The diet contained approximately 2400 calories, 100 grams of protein, 1 gram of calcium , and was low in residue. In Study I (3 days of bedrest and 3 days of bedrest with exercise) a two-day cycle menu of weighed and measured fresh foods was used. The composition of each of the two menus was secured through laboratory analysis of a sample tray prepared at the same time the trays were served to each subject. The same two-day menu cycle was used during the ambulatory periods and the last 5 days of the bedrest with exercise period of Study II. A three-day cycle menu of freeze-dried foods was used during the bedrest period of Study II and for the first 9 days of the bedrest with exercise period.[8] The chemical composition of the three menus of freeze-dried foods was known since analysis had been carried out by the manufacturer. Distilled water was the only liquid allowed in addition to the fluids of known calcium content that were given with each meal (coffee, tea, or milk).

E. Intake and output measurements

Each subject's intake and output were measured on a daily basis. The subjects were encouraged to drink all the liquids served with each meal. The amounts were known and recorded. Each additional intake of distilled water between meals was measured and recorded.

Each urine specimen was measured and the amounts were totaled for each period of collection. During the 3-day study all of the specimens voided by a subject were pooled from 12:00 noon of one day to 12:00 noon of the next. During the 14-day study the pooling of urine was from 7:00 a.m. to 7:00 p.m. and from 7:00 p.m. to 7:00 a.m. with the exception of the days of tilt when the specimens were pooled for the periods immediately preceding and following tilt.

Insensible water losses were not measured but they could be computed by making the following assumptions: 1) Insensible water loss equaled 45 ml. per 100 calories of caloric expenditure, and 2) Caloric expenditure in these subjects included 30 calories per kilogram to cover basal metabolism, 6 calories per kilogram to cover activity while in bedrest without exercise, and 4 calories per kilogram to cover specific dynamic action of foodstuffs. These assumptions are based on formulas available in the literature.[9] Provisions were made throughout the studies to record the presence and degree of visible sweating. Also, amounts lost through emesis were collected and measured in one instance when this occurred.

During the periods of collection, the specimens of urine were kept in individual jugs in a refrigerator located in the Immobilization Study Ward. At the end of each period of collection the bottles were sent to the laboratory where aliquot samples were taken for various urine chemistry analysis.

The subjects used a bedpan for excretion of stools. A plastic bag facilitated transfer of the fecal material from the bedpan to a glass jar of known weight that was properly labeled and sent to the laboratory for measurement and analysis. Carmine dye markers were used to identify the time of formation of the feces. Charcoal markers were used once but did not give sufficient color contrast to permit easy identification.

F. Bedside monitoring

The recording of physiological events was done every four hours throughout each period of the 3-day study and every twelve hours (7:00 a.m. and 7:00 p.m.) throughout each period of the 14-day study. On the seventh and eighth day of the first period of the 14-day study, physiological monitoring took place every four hours also.

The variables measured and recorded included the following: electrocardio-

gram, cardiotachogram, phonocardiogram, carotid pulse tracing, radial pulse, electrosphygmogram, and impedance pneumogram. These variables were displayed in an eight-beam oscilloscope and recorded on magnetic tape with adequate coding of the subject and time of monitoring. The magnetic tape records were played back on a direct recording instrument (a Physiograph or an Offner Dynograph) at a slow speed for quantification of the heart rate, respiratory rate and arterial blood pressure and at a fast paper speed for measurements of the duration of the cardiac cycle and its phases and for computation of the pulse wave velocity. The temperature was measured with an oral mercury thermometer and the values were recorded in a special source document.

During the 3-day study, the subjects had a permanently applied harness containing silver mesh electrodes that were placed across the chest for detection of the electrocardiogram and of the impedance pneumogram. The harness included also a blood pressure cuff with a piezoelectric crystal for detection of the Korotkoff sounds. Separate piezoelectric crystals for detection of the carotid and radial pulses and a microphone for recording the heart sounds were applied to each subject at each period of monitoring. The sensors were connected to a movable cabinet that contained the signal conditioners to process the physiological signals. During the 14-day study all of the electrodes and sensor devices were placed on each subject at each session of monitoring. A detailed description of the physiological monitoring system will be reported separately.

G. Metabolic balance studies

In order to carry out metabolic balance studies it was necessary to measure and to record the caloric, calcium, nitrogen, and phosphorus contents of the food eaten by every subject. This was done by analyzing a sample tray that contained the same food given to the subjects at each meal. Whenever an individual subject did not eat all the items on the tray, the refused contents were sent also to the laboratory for analysis. It was thus possible to compute the exact amount consumed by every subject.

The daily urinary output of the same metabolic products was calculated by analyzing the urine specimens. The intestinal excretion of these products was accounted for by chemical analysis of pools of feces collected through each period of study. On the eighth day of bedrest of Study II Subject T. G. O. (TIRR # 70012) had an emesis. Most of the vomitus was recovered and sent to the laboratory for measurement and analysis.

H. X-ray densitometry studies

Measurements of bone densitometry were made utilizing a technique developed by Dr. Pauline Mack of the Nelda Childers Laboratory for Human Nutrition Research of Texas Woman's University. X-ray films of the lumbar spine and the os

calcis were taken with special precautions to avoid undue irradiation of the subjects. In Study I the films were obtained immediately before and immediately after each period of recumbency and throughout the period of recovery following bedrest. In Study II radiographs were taken before bedrest, at different intervals during the period of recumbency, and throughout the days of recovery. The procedure, as carried out during the days of bedrest, did not jeopardize the keeping of the subjects in the horizontal position. The bed was moved to the X-ray area and it was placed at the side of the X-ray table which was the same height as the bed. The subject was assisted in rolling over from the bed to the table.

The films were processed and analyzed according to the technique that has been reported previously.[10] The results of this analysis of the density of the bone were related to the urinary output of calcium and phosphorus of these subjects. For this reason, aliquot samples of each pool of urine were sent to the Nelda Childers Laboratory for analysis of their calcium and phosphorus contents.

I. Passive tilt tests

At the beginning and at the end of each period of recumbency, a passive tilt test was performed on each subject. The details of the tilt procedure are given in a separate report.[11] . The electrodes and sensor devices used for bedside physiological monitoring were also applied to record the physiological data during tilt. A motorized tilt table changed the subject's position from 0° to 70° (feet down) in approximately 35 seconds. In the tilt posture the subject was suspended at the crotch by a built-in saddle, thus eliminating the need for foot support. The duration and sequence of the tilt procedures were varied in the two studies according to the respective protocols.

Samples of venous blood were obtained from the dorsum of the hand of each subject immediately before tilt, at the end of the period in the upright position, and fifteen minutes after return to the horizontal position. These samples of blood were analyzed for their 17-OH corticoid content. These studies were carried out on each of the four days of tilt of Study II.

J. Biochemical measurements

The experimental design called for numerous hematologic and biochemical measurements at different times before, during, and after each period of bedrest. The number and types of tests varied from study to study in accordance with the protocol requirements. In general, there were more blood tests done per day in Study I than in Study II, although the blood volume determinations were done more frequently in the 14-day study. Laboratory technicians collected blood samples through venous punctures at the pre-established intervals. The experimental design required frequent measurements of blood corticoids and other substances during the seventh and eighth days of the first period of 14 days bedrest. In order to obtain the blood samples with

minimum disturbance of the subject, a siliconized rubber catheter was inserted into the basilic or cephalic veins of the forearm and blood was aspirated through this catheter when required. The device, however, was not tolerated by Subject A.C.L. (TIRR # 70011) who preferred venous punctures to the permanent catheter. After withdrawal, the blood samples were placed in plain or oxalated test tubes as required for the specific type of analysis.

The urine, fecal, and food chemical analyses were carried out on samples collected according to the procedure indicated previously.

Hemoglobin determinations and reticulocyte counts were done to monitor the possible deleterious effect of repeated blood collections. Table 2 indicates the laboratory tests and techniques that were used throughout both studies.

K. General metabolism studies

In order to study the effects of immobilization on general metabolism, the O_2 consumption and CO_2 elimination were measured under conditions as close to basal as possible in the early morning hours throughout the three days of bedrest of Study I. These measurements allowed for computation of the respiratory exchange ratio of the subjects.

L. Ergometry tests

Before and after each period of bedrest of Study II, the subjects underwent an ergometry test to measure the cardiovascular response of the subjects to physical exercise. The test was carried out with a Lanooy bicycle ergometer. The design of this instrument is such that variations within a certain range in the rate of pedaling are compensated to result in a constant work load. Physiological monitoring of the electrocardiogram, the phonocardiogram, and the impedance pneumogram were done continuously before, during, and after the exercise. Each subject performed the exercise at increasing work loads until the heart rate reached approximately 170 per minute. Samples of expired air were collected with Douglas bags at different times throughout the exercise and the samples were analyzed for O_2 and CO_2 contents. The details of this test are reported separately.[12]

M. Isometric exercises

Every subject did isometric exercises regularly throughout the second period of bedrest of each study. The subject performed a thrust force between the heels and the shoulders on a thrust rack which lay on the bed surface. Levels of force to be produced by each subject were determined in advance and assigned individually according to the subject's weight and his performance during training sessions before bedrest. The amount of force exerted in each effort was measured and recorded. An auxilliary meter showed the subject how much force he had exerted. The subject

TABLE 2

LABORATORY TECHNIQUES

Test	Technique
Urine Calcium	Ferro and Ham (after dry ashing)
Serum Calcium	Flame Photometry
Fecal Calcium	Ferro and Ham (after dry ashing)
Urine Phosphorus	Fiske and SubbaRow
Fecal Phosphorus	Fiske and SubbaRow (after dry ashing)
Food Phosphorus	Fiske and SubbaRow (after dry ashing)
Urine Nitrogen	Kjeldahl
Fecal Nitrogen	Kjeldahl
Food Nitrogen	Kjeldahl
Plasma 17-OH Corticoids	Porter Silber (modified)
Urine 17-OH Corticoids	Peterson (modified)
RISA Blood Volume	Fields and Seed
Serum Glucose	Somogyi-Nelson
Lipid Absorption	Kunkel, Ehrens, and Eisenmenger
Fecal Water Content	Direct Drying
Reticulocyte Count	Brecker, G. and Schneiderman, M.
Serum Alkaline Phosphatase	Nitrophenyl Phosphate
Urine Creatinine	Folin and Wu; Bonsnes and Tausky
Serum Lactic Acid Dehydrogenase	Berger and Broida
Sodium	Flame Photometry
Potassium	Flame Photometry
Chloride	Schales and Schales
MHMA	Pisano, Crout and Abraham

remained in the supine horizontal position at all times and only a minor degree (10-15°) of knee flexion was required to produce the thrust force. The technique and apparatus will be described separately.[13]

Each run of exercise lasted five minutes and included efforts of five seconds with rest intervals of equal duration. There were four runs a day at two hour intervals. In the second bedrest period there were six runs a day at two hour intervals. Physiological monitoring through the exercise procedure was done in two consecutive days in each period of study.

TASK ASSIGNMENTS

The complexity of the experimental design and the intervention of numerous persons required coordination of efforts and careful assignments of tasks. There was need to instruct adequately the personnel who were to assist in the studies. A total of 29 professionals and 26 non-professionals participated actively.

In order to facilitate understanding of the tasks, written instructions describing specific procedures were circulated. It was necessary also to prepare a master protocol that was made available to all participants and that indicated clearly the tasks that needed completion and the person responsible for it. The master protocols and the instruction sheets for each procedure are included in the Appendix.

ANALYSIS OF RESULTS

The complexity of the experimental design and the numerous measurements anticipated for each study indicated the need to provide for a system for processing, storing, and retrieving the data collected in the course of the studies. Data pertaining to the subject's identification, past medical history, and physiological and sociological behavior during the study were entered into punch cards. Source documents of fixed format were used for collecting data at the bedside and in the laboratories. Analog to digital conversion was achieved by means of digitizers operated manually. Several computer programs were written that permitted application of mathematical and statistical models to the analysis of the data collected. The choice of models was the responsibility of the investigators in charge of specific areas of study.

The implementation of the system for data processing was simplified by utilizing some routine techniques used at the Texas Institute for Rehabilitation and Research. A separate report [14] gives a detailed description of the system.

REVIEW OF PROGRESS

It was necessary also to provide for a procedure that would allow the investigators to review periodically the progress of the studies. Diagrams prepared according to the guidelines of the Program Evaluation Review Technique (PERT)[15] were helpful in determining the status of each task at any one time. Figures 3 through 5 show the diagrams pertaining to each study. The major steps in this process of evaluation included: 1) Several conferences between the technical monitor of the Crew Systems Division of NASA Manned Spacecraft Center and the investigators of the Texas Institute for Rehabilitation and Research to set up the experimental design prior to Study I; 2) A conference held at the Texas Institute for Rehabilitation and Research on July 11, 1963, to evaluate the results available at the end of Study I. The technical monitor and the investigators participated in this conference; 3) A conference held on July 12, 1963, to set up the experimental design for Study II; 4) Regular meetings of the investigators of the Texas Institute for Rehabilitation and Research (and on some occasions with the technical monitor of NASA) at about two week intervals to review the results of the second study and to set up the objectives for future investigations; 5) A general conference with the investigators of the Texas Institute for Rehabilitation and Research, the technical monitor of NASA, and consultants of NASA to review the results of Studies I and II. This conference was held at the Manned Spacecraft Center of NASA on January 27, 1964; 6) Preparation of written reports of the results obtained in Studies I and II.

RESULTS

There is need to delineate the physiological effects of weightlessness in order to anticipate and prevent deleterious effects of space flights. To some extent bedrest in the horizontal position simulates the conditions of weightlessness. In spite of existing knowledge on the effects of prolonged bedrest, there is need to study further some of the consequences of immobilization and their mechanisms. For this reason, an Immobilization Study Unit was organized at the Texas Institute for Rehabilitation and Research under contract with the Manned Spacecraft Center of NASA. During 1963, a pilot experiment and two studies were conducted in order to: a) quantitate the degree of cardiovascular deconditioning resulting from 3 days and 14 days of bedrest, b) investigate the mechanisms of orthostatic hypotension, c) evaluate the information provided by indirect techniques of measurement of the cardiac cycle and its phases, d) measure the degree of bone demineralization, and e) evaluate the possible effect of isometric exercises during bedrest in preventing cardiovascular deconditioning and bone demineralization. This report gives a detailed description of the plan of study, the subjects selected, and the experimental conditions of the studies. The Appendix includes a detailed master protocol and descriptions of the techniques and procedures. The results of the studies are presented and discussed in separate reports.

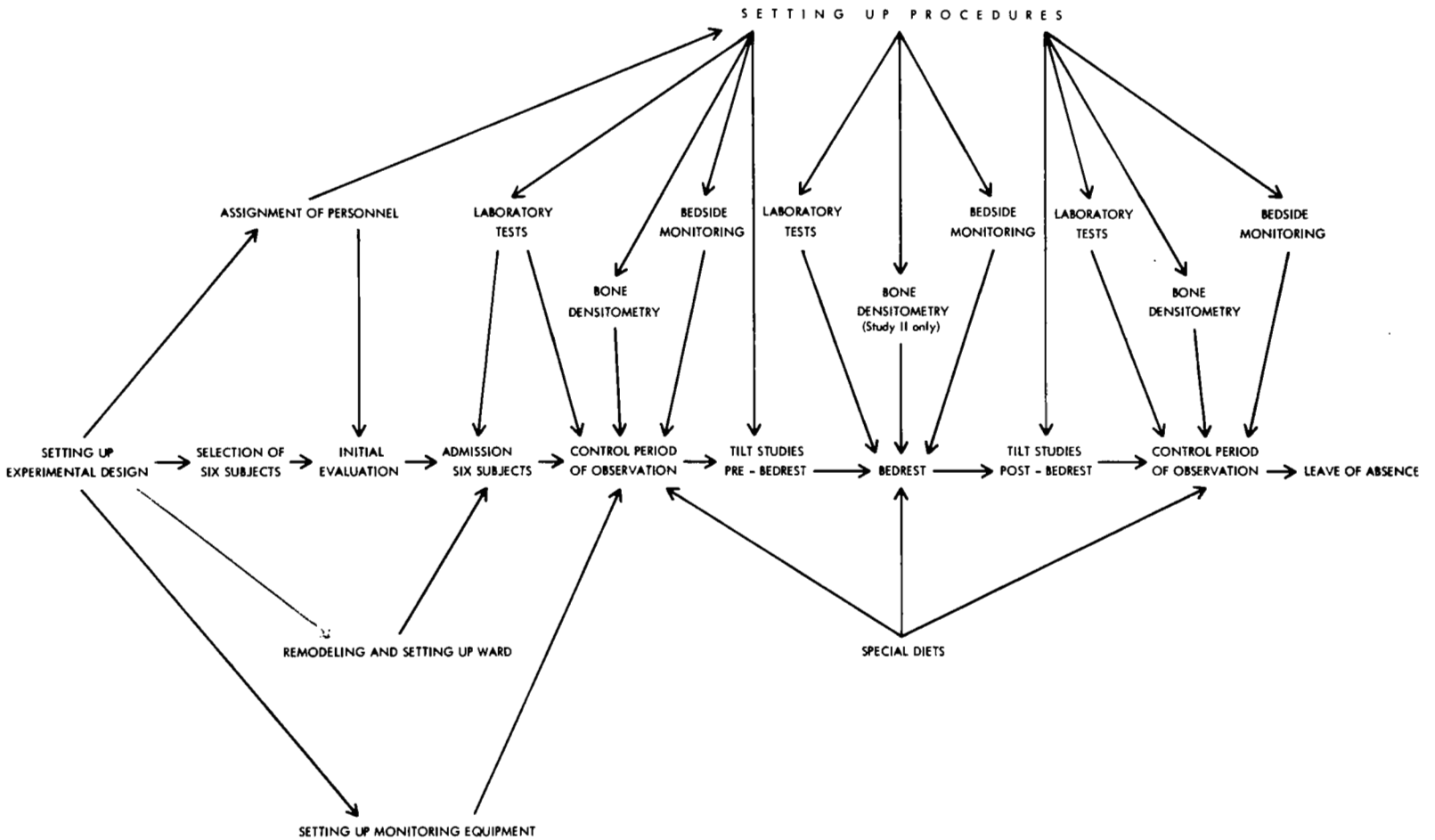


Figure 3. Diagram of the major tasks required for the bedrest periods of Study I and Study II.

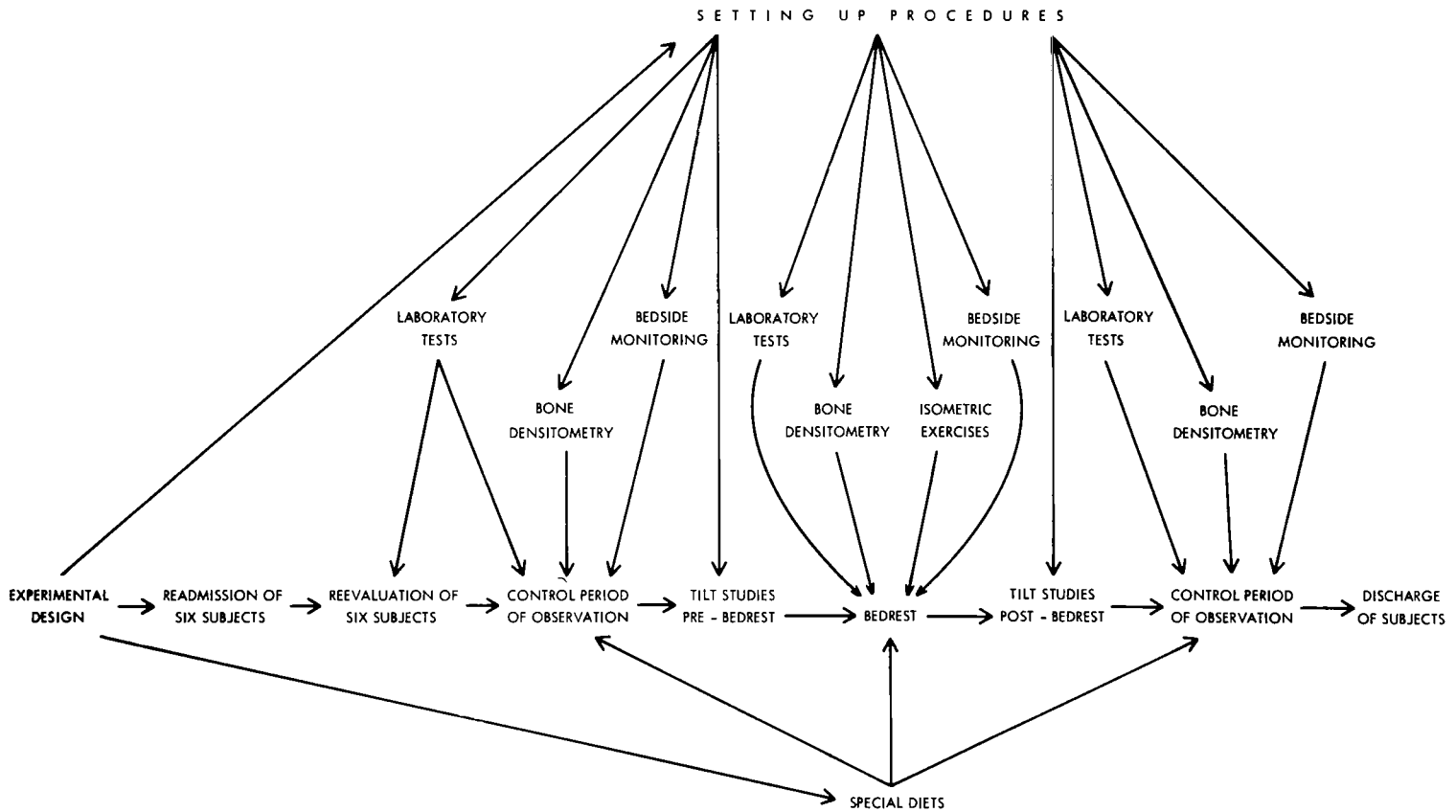


Figure 4. Diagram of the major tasks required for the bedrest with exercise periods of Study I and Study II.

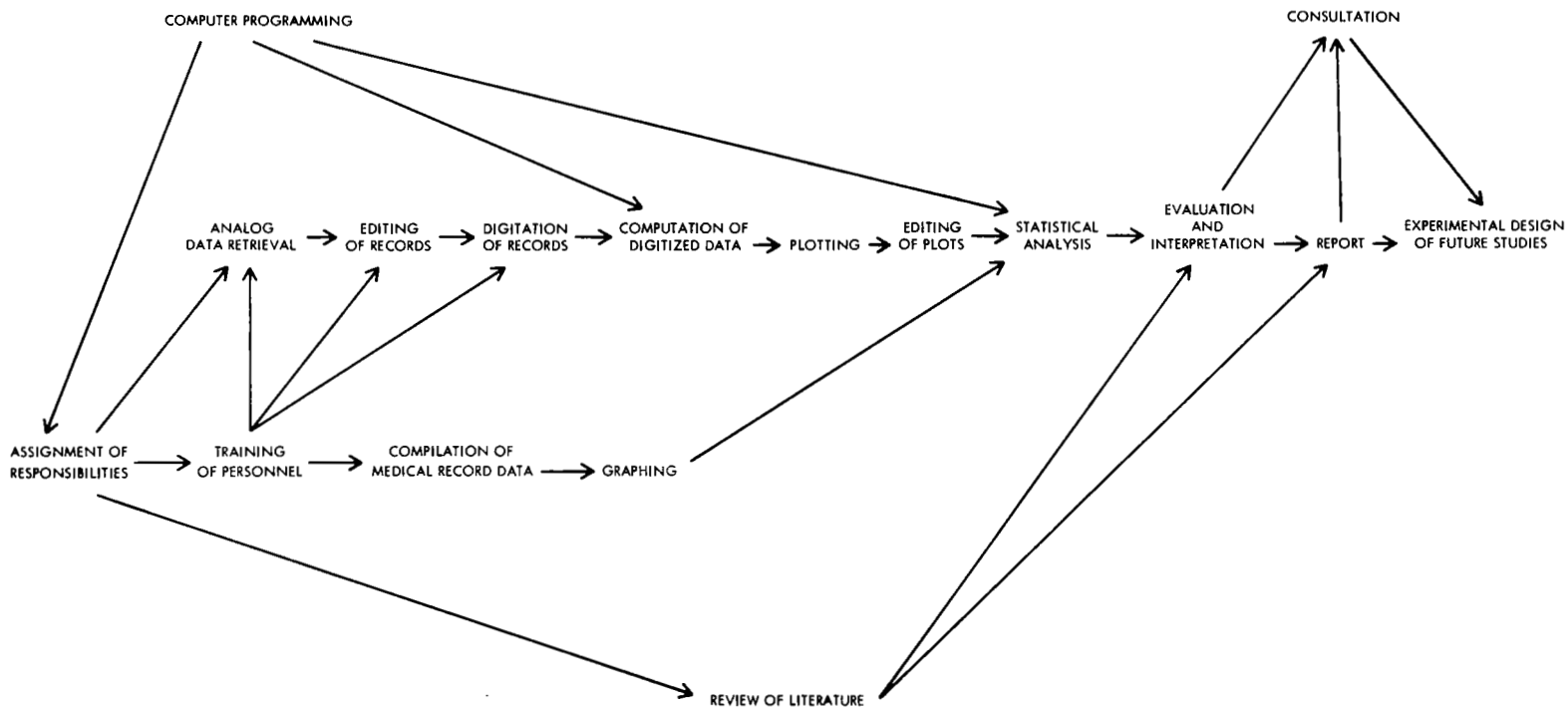


Figure 5. Diagram of the major tasks required for data analysis and review of the results of Study I and Study II.

REFERENCES

1. Vallbona C., Vogt, F. B., Cardus, D., Spencer, W. A., and Walters, M.: The Effect of Bedrest on Various Parameters of Physiological Function. I. A Review of the Literature on the Physiological Effects of Immobilization. NASA CR-171.

2. Gauer, O. H., and Haber, H.: Man under Gravity-free Conditions. German Aviation Medicine, World War II, Volume I, page 641, 1950.

3. Clark, C. C., Hardy, J. D.: Gravity Problems in Manned Space Stations. Proceedings, Manned Space Station Symposium, Institute of Aeronautical Sciences, Los Angeles, p. 104, April 20, 1960.

4. Berry, C. A., Minners, H. A., McCutcheon, E. P., and Pollard, R. A.: Aeromedical Analysis. Results of the Third United States Manned Orbital Space Flight, October 3, 1962. NASA SP-12.

5. Catterson, A. D., McCutcheon, E. P., Minners, H. A., and Pollard, R. A.: Aeromedical Observations. Mercury Project Summary Including Results of the Fourth Manned Orbital Flight, May 15 and 16, 1963. NASA SP-45.

6. Mazetti, R. F., Lucas, D. B., and Ralston, H. J.: Effect of Immobilization of the Knee on Energy Expenditure during Level Walking. Technical Report #43, Biomechanics Laboratory, University of California, p. 5, August, 1961.

7. Vogt, F. B., Cardus, D., Vallbona, C., and Spencer, W. A.: The Effect of Bedrest on Various Parameters of Physiological Function. VI. The Effect of the Performance of Periodic Flack Maneuvers on Preventing "Cardiovascular Deconditioning" of Bedrest. NASA CR-176.

8. Walters, M. E., Vallbona, C., Cardus, D., Vogt, F. B., and Spencer, W.: The Effect of Bedrest on Various Parameters of Physiological Function. V. Dietary Requirements. NASA CR-175.

9. Pickering, D. E., and Fisher, D. A.: Fluid and Electrolyte Therapy; A Unified Approach. Portland, Oregon: Medical Research Foundation of Oregon, 1959.

10. Mack, P. B., Vose, G. P., Nelson, J. D.: New Development in Equipment for the Roentgenographic Measurement of Bone Density. Am. J. Roentg. 82:303-10, August, 1959.

11. Vallbona, C., Cardus, D., Vogt, F. B., and Spencer, W. A.: The Effect of Bedrest on Various Parameters of Physiological Function. VIII. The Effect on the Cardiovascular Tolerance to Passive Tilt. NASA CR-178.

12. Cardus, D., Spencer, W. A., Vallbona, C., and Vogt, F. B.: The Effect of Bedrest on Various Parameters of Physiological Function. VII. Cardiac and Ventilatory Response to the Bicycle Ergometer Test. NASA CR-177.

13. Vogt, F. B., Mack, P. B., Beasley, W. C., Spencer, W. A., Cardus, D., and Vallbona, C.: The Effect of Bedrest on Various Parameters of Physiological Function. XII. The Influence of Bedrest Immobilization on Calcium Balance and Bone X-ray Density. NASA CR-182.

14. Vallbona, C., Spencer, W. A., Blose, W., Cardus, D., Vogt, F. B., and Leonard, J.: The Effect of Bedrest on Various Parameters of Physiological Function. IV. A System for Processing Data Collected in the Immobilization Study Unit. NASA CR-174.

15. National Aeronautics and Space Administration: Systems Manual for NASA PERT. Houston, Texas: NASA, January, 1963.

APPENDIX

MASTER PROTOCOL -- BEDREST STUDIES

A Master Protocol was designed for the experimental studies conducted at the Texas Institute for Rehabilitation and Research (TIRR) to assure completion of all components of the study and to clearly define the responsible person for carrying out the procedures.

The following code was used to define the responsible person for each task:

AO - Admitting Office
CV - Carlos Vallbona, M.D.
D - Dietician
DC - David Cardus, M.D.
DK - Dick Kenyon, Photographer
E - Engineers
F - Mrs. Angela Fraga
HL - Harry Lipscomb, M.D.
K - Dr. Kirkham
L - Laboratory
Mc - Mr. McTaggart
M - Pauline B. Mack, Ph.D.
MM - Mrs. Maurine B. Mitchell, Social Service
O - Orderly
P - Physician on call or assigned
R - Radiology
S - Subjects
T - TIRR

APPENDIX A

COMPREHENSIVE EXPERIMENTAL PROTOCOL

THREE-DAY IMMOBILIZATION STUDY

Texas Institute for Rehabilitation and Research

Date		Procedure	Responsible
April			
30	Interview and selection of subjects		P
May			
1	12 noon	Start on special diet	D
	1 pm	Admission to hospital, history and physical examination	P
	6 pm	Dinner	D
	10 pm	Spend night at TIRR	S
2	8 am	Blood drawn	L
	8:30 am	Breakfast	D
	12 noon	Start 24-hour urine collection	O,S
	12:30 pm	Lunch, carmine dye capsule prior to lunch	D
	1 pm	Chest X-ray	T
	6 pm	Dinner	D
	10 pm	Spend night at TIRR	S
3	8 am	Blood drawn	L
	8:30 am	Breakfast	D
	11:50 am	Urinate	O,S
	11:55 am	Blood	L
	12 noon	Complete 24-hour urine collection	L,S
	12:30 pm	Lunch	D
	2:30 pm	Psychiatric interview	P
	4 pm	Blood	L
	6 pm	Dinner	D

CODE

P	Physician	R	Radiology
L	Laboratory	S	Subjects
D	Dietician	M	Dr. Mack
E	Engineers	O	Orderly
T	TIRR	B	Dr. Beasley

Date		Procedure	Responsible
4	8 am	Start final checkout of equipment including intra-arterial blood pressure	P,E
	8:30 am	Breakfast	D
	11:50 am	Urinate	O,S
	12 noon	Complete 24-hour urine collection	O,S
	12:30 pm	Lunch	D
	6 pm	Dinner	D
5	8 am	Weigh	O
	8:30 am	Breakfast	D
	11:55 am	Urinate	
	12 noon	Complete 24-hour urine collection	O,S
	12:30 pm	Lunch	D
	1 pm	Subject and harness check out	P,E,S
	2 pm	X-ray densitometry studies	M
	6 pm	Dinner	D
6	On May 6,1963, prior to immobilization, tilt studies were done on all subjects as indicated on schedule.		
	7 am - 8 am	Respiratory studies on all subjects	
	7:30 am	Weigh	O
	7:50 am	Isotope to be injected	R
	8 am	Blood to be drawn	L
	8:30 am	Breakfast	D
	11:50 am	Urinate	S,O
	12 noon	Complete 24-hour urine collection	S,O
		Blood to be drawn	L
	12:30 pm	Lunch, carmine dye capsule prior to lunch	D
	3 pm	Data, temperature	P,O
	4 pm	Blood to be drawn	L
	6 pm	Dinner	D
	7 pm	Data and temperature	P,O
	8 pm	Blood to be drawn	L
	11 pm	Data and temperature	P,O
	12 midn.	Blood to be drawn	L
7	3 am	Data and temperature	P,O
	7 am	Data and temperature	P,O
	7:50 am	Isotope to be injected	R

Date		Procedure	Responsible
7 - cont.	8 am	Blood to be drawn	L
	8:30 am	Breakfast	D
	9 am	Check electrode harness and measure resistance	E
	11 am	Data and temperature	P,O
	11:50 am	Urinate	S,O
	12 noon	Complete 24-hour urine collection	S,O
	12:30 pm	Lunch	D
	3 pm	Data and temperature	P,O
	6 pm	Dinner	D
	7 pm	Data and temperature	P,O
	11 pm	Data and temperature	P,O
8	3 am	Data and temperature	P,O
	7 am	Data and temperature	P,O
	7 am - 8 am	Respiratory studies on all subjects	
	7:50 am	Isotope to be injected	R
	8 am	Blood to be drawn	L
	8:30 am	Breakfast	D
	9 am	Check electrode harness and measure resistance	E
	11 am	Data and temperature	P,O
	12 noon	Urinate and complete 24-hour urine collection	S,O
	12:30 pm	Lunch	D
	3 pm	Data and temperature	P,O
	6 pm	Dinner	D
	7 pm	Data and temperature	P,O
	11 pm	Data and temperature	P,O
8	NOTE: Glucose determination tests were done on all subjects during pm on this date		L
9	3 am	Data and temperature	P,O
	7 am	Data and temperature	P,O
	7:50 am	Isotope to be injected	R
	8 am	Blood to be drawn	L
	8:30 am	Breakfast	D
	9 am	Check electrode harness and measure resistance	E
	11 am	Data and temperature	P,O

Date		Procedure	Responsible
9-cont.	12 noon	Urinate and complete 24-hour urine collection	S,O
	12:30 pm	Lunch	D
		Tilt studies (Pulse wave velocity)	
		Weigh at end of tilt studies	
	4 pm	X-ray densitometry studies	M
	6 pm	Dinner	D
10	7 am - 8 am	Respiratory studies on all patients	
	7:30 am	Weigh	O
	7:50 am	Isotope to be injected	R
	8 am	Blood to be drawn	L
	8:30 am	Breakfast	D
	11:50 am	Urinate	
	12 noon	Complete 24-hour urine collection	S,O
		Blood to be drawn	L
	12:30 pm	Lunch	D
	4 pm	Blood to be drawn	L
	6 pm	Dinner	D
	8 pm	Blood to be drawn	L
	12 midn.	Blood to be drawn	L
11	7:30 am	Weigh	O
	8 am	Blood to be drawn	L
	8:30 am	Breakfast	D
	11:50 am	Urinate	
	12 noon	Complete 24-hour urine collection	S,O
	12:30 pm	Lunch	D
	1 pm	Dismiss on leaves of absence until May 15, 1963 at 7:30 am	P,S
15	Subjects returned from leave. All subjects were placed on regular diet for this day.		
	1:30 pm	Interval physical and history	P
16	7:30 am	Weigh	O
	8 am	Blood to be drawn	L
	8:30 am	Breakfast (special diets start this date)	D
	11:30 am	Carmine dye markers	O
	12 noon	Urinate and discard, start 24-hour urine collection	S,O
	12:30 pm	Lunch	D
	6 pm	Dinner	D

Date		Procedure	Responsible
17	7:30 am	Weigh	O
	8 am	Blood to be drawn	L
	8:30 am	Breakfast	D
	11:50 am	Urinate	
	12 noon	Complete 24-hour urine collection	S,O
		Blood to be drawn	L
	12:30 pm	Lunch	D
	4 pm	Blood to be drawn	L
	6 pm	Dinner	D
	8 pm	Blood to be drawn	L
	12 midn.	Blood to be drawn	L
18	7:30 am	Weigh	O
	8:30 am	Breakfast	D
	11:50 am	Urinate	
	12 noon	Complete 24-hour urine collection	S,O
	12:30 pm	Lunch	D
	6 pm	Dinner	D
	NOTE: Preliminary isometric exercise instructions were started on this date		B,O
19	7:30 am	Weigh	O
	8:30 am	Breakfast	D
		X-ray densitometry studies were done on all subjects	M
	12 noon	Urinate and complete 24-hour urine collection	S,O
	12:30 pm	Lunch	D
		Isometric exercise instructions were completed on this date	B,O
	6 pm	Dinner	D
20	On May 20,1963, prior to immobilization, tilt studies were done on all subjects as indicated on schedule		
	7:50 am	Isotope to be injected	R
	8 am	Blood to be drawn	L
	8:30 am	Breakfast	D
	11:50 am	Urinate	
	12 noon	Complete 24-hour urine collection	S,O
		Blood to be drawn	L

Date		Procedure	Responsible
20 - cont.	12:30 pm	Lunch	D
	2:15 pm	Isometric exercise started	B,O
	4 pm	Blood to be drawn	L
	5 pm	Carmine dye marker	O
	6 pm	Dinner	D
	7 pm	Data and temperature	P,O
	8 pm	Blood to be drawn	L
	11 pm	Data and temperature	P,O
	12 midn.	Blood to be drawn	L
21	3 am	Data and temperature	P,O
	7 am	Data and temperature	P,O
	8 am	Blood to be drawn	L
	8:30 am	Breakfast	D
	9 am	Check electrode harness and measure resistance	E
	9:20 am	Isometric exercise (1st round)	B,O
	11 am	Data and temperature	P,O
	11:20 am	Isometric exercise (2nd round)	B,O
	12 noon	Urinate and complete 24-hour urine collection	S,O
	12:30 pm	Lunch	D
	1:35 pm	Isometric exercise (3rd round)	B,O
	3 pm	Data and temperature	P,O
	3:40 pm	Isometric exercise (4th round)	B,O
		Isotope injected	R
	6 pm	Dinner	D
	7 pm	Data and temperature	P,O
	11 pm	Data and temperature	P,O
22	3 am	Data and temperature	P,O
	7 am	Data and temperature	P,O
	7:50 am	Isotope to be injected	R
	8 am	Blood to be drawn	L
	8:30 am	Breakfast	D
	9 am	Check electrode harness and measure resistance	E
	9:30 am	Isometric exercise (1st round)	B,O
	11 am	Data and temperature	P,O
	11:35 am	Isometric exercise (2nd round)	B,O
	11:50 am	Urinate	
	12 noon	Complete 24-hour urine collection	S,O
		Blood to be drawn	L

Date		Procedure	Responsible
22 - cont.	12:30 pm	Lunch	D
	1:35 pm	Isometric exercise (3rd round)	B,O
	3 pm	Data and temperature	P,O
		Isometric exercise (4th round)	B,O
	4 pm	Blood to be drawn	L
	6 pm	Dinner	D
	7 pm	Data and temperature	P,O
	8 pm	Blood to be drawn	L
	11 pm	Data and temperature	P,O
	12 midn.	Blood to be drawn	L
23	3 am	Data and temperature	P,O
	7 am	Data and temperature	P,O
	7:50 am	Isotope to be injected	R
	8 am	Blood to be drawn	L
	8:30 am	Breakfast	D
	9 am	Check electrode harness and measure resistance	E
	8:45 am	Isometric exercise (1 round only, 30 minutes prior to tilt studies on each subject)	B,O
		Tilt studies begin	
		Weigh at end of tilt	
	11 am	Carmine dye markers following tilt	O
	11:50 am	Urinate and complete 24-hour urine collection	S,O
	12:30 pm	Lunch	D
		Movies during exercise and tilt studies	
	4 pm	X-ray densitometry studies	M
	6 pm	Dinner	D
24	7:30 am	Weigh	O
	7:50 am	Isotope to be injected	R
	8 am	Blood to be drawn	L
	8:30 am	Breakfast	D
	9 am	X-ray densitometry studies completed	M
	11:50 am	Urinate and complete 24-hour urine collection	S,O
	12 noon	Blood to be drawn	L
	12:30 pm	Lunch	D
	4 pm	Blood to be drawn	L
	6 pm	Dinner	D
	8 pm	Blood to be drawn	L
	12 midn.	Blood to be drawn	L

Date		Procedure	Responsible
25	7:30 am	Weigh	O
	8:30 am	Breakfast	D
	11:30 am	Carmine dye marker	O
	12 noon	Urinate and complete 24-hour urine collection	S,O
	12:30 pm	Lunch	D
	1 pm	All subjects discharged	P

INITIAL INTERVIEW, PHYSICAL EXAMINATION AND HISTORY

1. All prospective candidates for the study must be interviewed by a physician.

2. At the time of the interview, the subjects will be acquainted in general terms with the experimental design, with the purposes of the study and the possible risks involved.

3. Each subject shall be selected on the basis of his age, current health, past medical history and psychological fitness.

4. A complete history shall be taken and a complete physical examination shall be done by the physician prior to accepting the subject for the study.

5. The initial evaluation shall include:

   a. Statement of present physical condition
   b. Statement of current psychological fitness
   c. A detailed past medical history
   d. A review of systems
   e. A detailed family history
   f. A detailed statement regarding current habits (eating, smoking, drinking, sleeping, exercise, etc.)

6. The physical examination shall be complete and it shall include an examination of:

   a. General appearance, skin, lymphatic system, head, eyes-ears-nose and throat, neck, spine, chest (lungs and heart), abdomen, genitalia, extremities, and neurological. Chest X-rays will be done on each subject.

7. An evaluation of the psychological condition of the subject shall be made by a consultant psychiatrist.

8. An evaluation of the sociological conditions surrounding the subject shall be done by the medical social worker.

9. Each subject shall sign the proper forms and authorizations of release and relinquishing responsibility prior to active participation in the study.

10. Each subject will be admitted to the TIRR through routine procedures for admittance of all patients. Standard admitting forms will be used.

FOOD ANALYSIS PROCEDURE

All subjects were started on special diets on May 1,1963, at 12 noon for first study. All subjects were started on special diets on May 16, 1963, at 8:30 am for the second study.

1. Subjects shall be on identical carefully controlled diets, shall be required to eat ALL food served, and shall take no additional food.

2. An extra meal shall be prepared by dietician and saved for food analysis.

3. Servings from lunch, dinner and breakfast (the next morning) shall be pooled to represent diet for each 24 hour period.

4. Weight of food shall be recorded.

5. Food shall be analyzed daily for:

   a. Calcium b. Phosphates c. Nitrogen

6. Food Analysis Source Document shall be filled out for each subject for each day.

7. The diets for the two periods of study contained 2,500 calories per day, 1 gm. of calcium and 75 gms. of protein and a low residue.

NUTRITIONAL INTAKE PROTOCOL

1. Each subject shall be on a special diet containing a predetermined amount of calories, minerals and residue.

2. Liquids taken with meals shall be included in the tray prepared for chemical analysis. Between meals each subject may drink distilled water only.

3. Each subject shall be required to eat all food served and shall take no additional food.

INTAKE AND OUTPUT PROCEDURES

A. INTAKE PROTOCOL

1. All food and liquid intake for each subject shall be recorded in the special source documents.

2. The amount of liquid taken shall be measured exactly. In order to facilitate this measurement, cups measuring eight (8) ounces will be available and when a subject asks for a drink of water he shall be offered a full cup containing eight (8) ounces. Whatever amount is left after drinking shall be measured exactly in order to compute the amount taken.

3. Each subject shall be asked to eat all food contained on the tray offered to him at each meal. All fluid offered with meals shall be taken in by all subjects.

4. In the event that a subject is unable to ingest all the food or liquid offered on his tray, the amounts left over shall be put back on the tray and sent to the laboratory for measurement and analysis.

B. OUTPUT PROTOCOL

1. Solid and liquid output of each subject shall be collected according to specifications given in the protocols for urine collection and also for fecal collections.

2. If the subject perspires during the period of Immobilization, a statement regarding the amount of perspiration shall be included in the source documents of clinical observations.

3. A rating will be made of the degree of perspiration according to the following scale: a. trace, b. fair amount, c. moderate amount, d. large amount, e. profuse.

4. If the subject vomits during the period of study, the attending physician shall be notified immediately. The whole amount of vomitus shall be collected if possible and sent to the laboratory for measurement and analysis.

5. The total amount of blood collected on each subject for blood chemical analysis shall be entered in the intake and output record.

BLOOD COLLECTION PROCEDURES

CODE	
Blood Tests	**Blood Bottles**
a. Calcium	1. 10 cc. Using heparinized syringe
b. Phosphorus	2. 6 cc. (Stopped bottle, clotted)
c. Alkaline phosphatase	3. 2-3 cc. Oxalate
d. Osmolarity	4. 15 cc. (Clotted)
e. Na	5. 3 cc. Oxalate
f. K	6. 2 cc. (Clotted)
g. Cl	7. 5 cc. (Clotted)
h. CO_2	8. 10 cc. (Clotted)
i. Hb	
j. Hct	
k. WBC	
l. Serology	
m. 17-OH	
n. Blood volume	
o. Protein electrophoresis	
p. Blood urea nitrogen	
q. Lactic acid dehydrogenase	

Date	Time	Test	Blood to be Drawn	Comments
May				
2	8 am	abcdefghijklop	2,3,4	
3	8 am	mq	1,6	
	12 noon	mq	1,6	
	4 pm	mq	1,6	
	8 pm	mq	1,6	
	12 midn.	mq	1,6	
6	7:50 am	n	5	Draw and inject isotope
	8 am	abcdefghijkq	2,3,8	Draw from opposite arm
	12 noon	m	1	
	4 pm	m	1	
	8 pm	m	1	
	12 midn.	m	1	

Date	Time	Test	Blood to be Drawn	Comments
7	7:50 am	n	5	Draw and inject isotope
	8 am	abcijkpqm	1,3	Draw from opposite arm
8	7:50 am	n	5	Draw and inject isotope
	8 am	abcijkpq	3,7	Draw from opposite arm
	12 noon	mq	1,6	
	4 pm	mq	1,6	
	8 pm	mq	1,6	
	12 midn.	mq	1,6	
9	7:50 am	n	5	Draw and inject isotope
	8 am	abcdefghijkmopq	1,2,3,8	Draw from opposite arm
10	7:50 am	n	5	Draw and inject isotope
	8 am	abcdefghijkmop	1,2,3,7	Draw from opposite arm
	12 noon	m	1	
	4 pm	m	1	
	8 pm	m	1	
	12 midn.	m	1	
11	8 am	q	6	
16	8 am	abcdijkop	3,8	
17	8 am	abcijkm	1,3,7	
	12 noon	m	1	
	4 pm	m	1	
	8 pm	m	1	
	12 midn.	m	1	
20	7:50 am	n	5	Draw and inject isotope
	8 am	abcdijkop	3,8	Draw from opposite arm
	12 noon	m	1	
	4 pm	m	1	
	8 pm	m	1	
	12 midn.	m	1	
21	7:50 am	n	5	Draw and inject isotope
	8 am	abcijkmp	1,3,7	Draw from opposite arm

Date	Time	Test	Blood to be Drawn	Comments
22	7:50 am	n	5	Draw and inject isotope
	8 am	abcijkp	3,7	Draw from opposite arm
	12 noon	m	1	
	4 pm	m	1	
	8 pm	m	1	
	12 midn.	m	1	
23	7:50 am	n	5	Draw and inject isotope
	8 am	abcdijkmop	1,3,8	Draw from opposite arm
24	7:50 am	n	5	Draw and inject isotope
	8 am	abcdijkmop	1,3,8	Draw from opposite arm
	12 noon	m	1	
	4 pm	m	1	
	8 pm	m	1	
	12 midn.	m	1	
25		Subjects Discharged		

URINE COLLECTION PROCEDURES

Date	Time	Test	Comment
May			
2	11:30 am	2	
2 - 3	12 noon to 12 noon	1,4	
3 - 4	12 noon to 12 noon	1	
4 - 5	12 noon to 12 noon	1,6	
5 - 6	12 noon to 12 noon	1	
6 - 7	12 noon to 12 noon	1,4,6	
7 - 8	12 noon to 12 noon	1,6	
8 - 9	12 noon to 12 noon	1,4	
9 - 10	12 noon to 12 noon	1,4,6	
10 - 11	12 noon to 12 noon	1	
15	Subjects returned from leave		
16 - 17	12 noon to 12 noon	1,4	
17 - 18	12 noon to 12 noon	1,6	
18 - 19	12 noon to 12 noon	1	
19 - 20	12 noon to 12 noon	1	
20 - 21	12 noon to 12 noon	1,4,6	
21 - 22	12 noon to 12 noon	1	
22 - 23	12 noon to 12 noon	1,4,6	
23 - 24	12 noon to 12 noon	1,4	
24 - 25	12 noon to 12 noon	1,6	All subjects discharged

CODE FOR TESTS

1. Ca, P., N., Creatinine
2. Routine and microscopic
4. Na., K., Cl., Osmolarity
6. 17-OH Steroids -- to be sent to Dr. Eik-Ness, Salt Lake City, Utah

URINE HANDLING PROCEDURES

1. All urine samples shall be pooled for a 24-hour period (12 noon of one day until 12 noon of the following day) unless specifically indicated otherwise.

2. Urine shall be collected in iced containers.

3. Urine shall be covered to prevent exposure to light.

4. The 24-hour urine samples shall be utilized for various chemical determinations. However, certain information and procedures are required for each voiding.

5. During immobilization, the following shall be recorded on intake-output sheets for EACH VOIDING.

   a. Time.
   b. Measure and record specific gravity (return the sample to container after measurement is made).
   c. Measure and record volume.
   d. Test urine sample for sugar using 5 drops of urine, 5 drops of water, and a clinitest tablet, note color and compare with chart and record results.

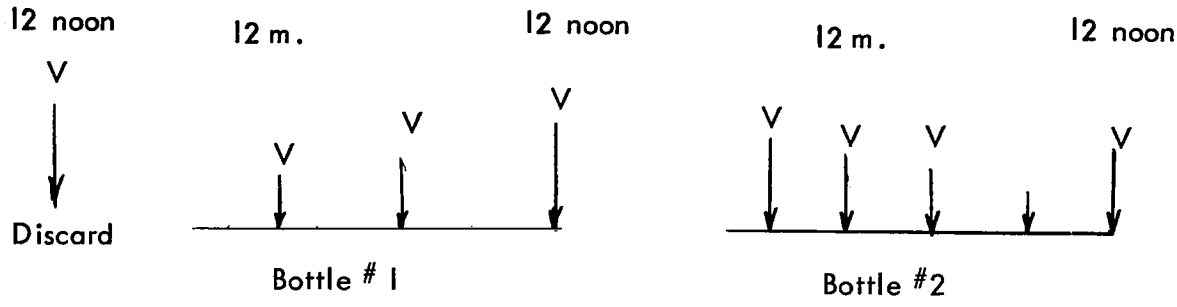
   ATTENTION: If positive for even a trace amount of sugar, notify physician on call and a blood sugar will be drawn.

   e. Put entire sample in container for 24-hour pooling.

6. During pre-immobilization and post-immobilization, omit Step 5,d.

7. To start 24-hour collection, proceed as follows:

   a. Have subject urinate and discard sample at 12 noon of assigned day.
   b. Then, for each and every voiding between 12 noon of assigned day and 12 noon of following day, save all urine voided and test as indicated in Steps 5 and 6.
   c. At 12 noon, have subject void (whether he thinks he has to or not) and put in bottle for preceding day.
   d. The urine from successive voidings are put in the next day's bottle which will also include urine from the noon voiding of the next day.
   e. See graph on next page.



8. Subjects shall be instructed to empty their bladder (and keep sample) prior to having a bowel movement to prevent mixing of urine and feces.

9. At the end of the 24-hour period of collection, the untreated, cooled urine shall be divided, labeled, and processed as follows:

   a. Shake carefully.
   b. Measure and record total volume.
   c. Measure and record specific gravity.
   d. Divide the urine samples into separate bottles as shown below, labeled with: subject's name, date, time of collection, subject number, and total 24-hour volume.

      1) 50 ml - untreated: MACK, UTAH (where indicated)
      2) 200 ml - untreated: MACK
      3) 200 ml - treated: MACK (where indicated)
      4) ml - untreated: TIRR determinations
      5) ml - treated with 6N HCL

   e. After dividing, put urine in freezer in compartments marked: UTAH, MACK and TIRR.

FECAL COLLECTION PROCEDURES

1. Give marker (0.5 gram carmine capsule) just before lunch on Thursday, May 2, 1963. (Beginning of secand day)

   Collect feces beginning when marker first appears up to the next marker.

2. Give marker again just before lunch on Monday, May 6,1963. (Beginning of immobilization)

   Collect feces from beginning of second marker up to third marker.

3. Give third marker just before lunch on Thursday, May 9,1963. (End of immobilization)

   Collect feces from beginning of third marker up to fourth marker.

4. Give fourth marker just before lunch on Saturday, May 11, 1963.

5. All feces for any one period are pooled in one quart jar (pre-weighed). If necessary, use a second jar.

6. Subjects are all to take feces collecting container home with them and shall collect during this time until the appearance of the last dye marker. This shall be returned to TIRR in a bag and placed in the special refrigerator in the laboratory.

PREPARATION FOR TILT

Schedule for May, 1963: All subjects went through tilt testing as indicated on the previous page.

Time (Approximate)	Subject No.	5/6/63 & 5/9/63	5/20/63 & 5/23/63
8 am - 9 am	1	Westerlage	McAnally
9:30 am - 10:30 am	2	Willard	Swearingen
11:00 am - 12 noon	3	Lawson	Brown
1 pm - 2 pm	4	Brown	Lawson
2:30 pm - 3:30 pm	5	Swearingen	Willard
4 pm - 5 pm	6	McAnally	Westerlage

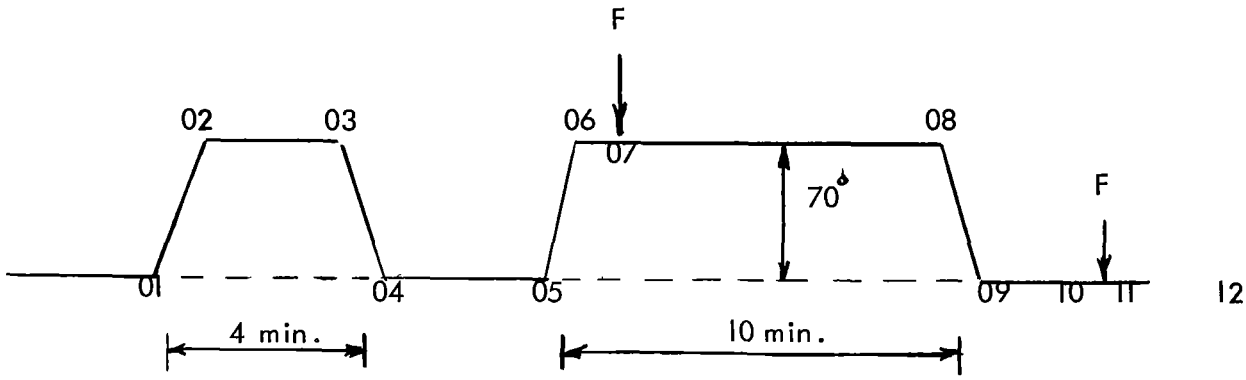
One half-hour prior to tilt, each subject had his own electrode harness applied (or checked) and intra-arterial needle inserted.

Throughout the passive tilt test the electrocardiogram, the pneumogram, the carotid pulse, the radial pulse, the phonocardiogram, the intra-arterial pressure and Korotkoff sounds in the brachial artery during intermittent inflation of a cuff were monitored. During the Flack test, the phonocardiogram was not recorded in order to register the pressure in the airway of the subject.

PASSIVE TILT TESTING

Passive tilt testing was done on May 6, 9, 20 and 23, as indicated on the calendar representation of studies.

The duration of stay in the tilt position was changed in some subjects depending on their cardiovascular tolerance.



CODE OF SITUATION

F	Flack Test
01	Steady state, supine position 0°
02	Reaching 70°
03	Steady state 70°
04	Reaching 0°
05	Steady state 0°
06	Reaching 70°
07	End Flack at 70°
08	Steady state 70°
09	Reaching 0°
10	Steady state 0°
11	End Flack 0°
12	Steady state 0°

MONITORING PROCEDURES

A. BEDSIDE MONITORING

1. Each subject shall have chronically implanted electrodes for recording of the electrocardiogram and pneumogram.

2. Pick-ups for recording other physiological variables will be attached to each subject prior to each period of recording, depending on the experimental design.

3. The electrodes and pick-ups shall be connected to the movable cabinet and from there they shall be transmitted by connecting cable to a console where the variables will be displayed on an oscilloscope and permanently recorded on magnetic tape.

4. The duration of the recordings and the time frequency of the recordings will vary according to each phase of the study and the experimental design.

5. Information pertaining to the subject being monitored at the time will be properly coded on magnetic tape.

B. PHYSIOLOGICAL MONITORING DURING IMMOBILIZATION

1. During the two periods of immobilization the following physiological variables were monitored over a period of three to five minutes: electrocardiogram, phonocardiogram, carotid pulse, radial pulse, pneumogram, and Korotkoff sounds at the brachial artery during intermittent cuff inflation.

2. Each subject was monitored at regular intervals during the period of immobilization. The first monitoring took place at 7 pm on May 6, 1963, and was repeated every four hours until the last monitoring at 7 am on May 9, 1963. During the second phase of the immobilization, the first monitoring took place at 7 pm on May 20,1963, and was repeated every four hours until 7 am on May 23, 1963.

3. On May 21 and 22, 1963, a physiological monitoring of the subjects was carried out during exercise beginning at 11:10 am and 3 pm respectively.

GENERAL METABOLISM STUDIES

In order to study the effects of immobilization on general metabolism, oxygen consumption will be measured under conditions as close to basal conditions as possible. A sample of expired air will be collected in Douglas bags for two minutes on each subject at regular intervals of time during the period of immobilization.

Gas volume measurements will be performed with the dry gas meter and samples will be analyzed for CO_2 and O_2 according to the micro technique of Scholander. The results will be reported on the source document for Gas Exchange studies.

ISOMETRIC EXERCISE DURING BED REST

	Round 1	Round 2	Round 3	Round 4
Saturday, May 18, 1963				
R.N. McA., # 70-0-07		Trial Runs, am		
W.R.S., # 70-0-08				
R.K.W., # 70-0-01				
C.B.B., # 70-0-06				
Sunday, May 19, 1963				
R.G.W., # 70-0-10		Trial Runs, am		
T.H.L., # 70-0-09				
Monday, May 20, 1963				
R.N. McA., # 70-0-07	2:15 pm			
W.R.S., # 70-0-08	2:30 pm			
C.B.B., # 70-0-06	2:35 pm			
T.H.L., # 70-0-09	2:50 pm			
R.K.W., # 70-0-01	3:06 pm			
R.G.W., # 70-0-10	3:50 pm			
Tuesday, May 21, 1963				
R.N. McA., # 70-0-07	9:20 am	12:10 pm*	2:20 pm	4:20 pm
W.R.S., # 70-0-08	9:35 am	12 noon*	2:15 pm	4:15 pm
C.B.B., # 70-0-06	9:45 am	11:48 am*	2:05 pm	4:05 pm
T.H.L., # 70-0-09	9:50 am	11:35 am*	2:00 pm	3:45 pm
R.G.W., # 70-0-10	10:00 am	11:25 am*	1:50 pm	3:40 pm
R.K.W., # 70-0-01	10:10 am	11:10 am*	1:35 pm	3:55 pm
Wednesday, May 22, 1963				
R.N. McA., # 70-0-07	10:20 am	12:10 pm	2:12 pm	4:15 pm*
W.R.S., # 70-0-08	10:15 am	12 noon	2:05 pm	4:10 pm*
C.B.B., # 70-0-06	10:00 am	11:53 am	1:58 pm	3:45 pm*
T.H.L., # 70-0-09	10:55 am	11:45 am	1:50 pm	3:30 pm*
R.G.W., # 70-0-10	9:45 am	11:40 am	1:45 pm	3:15 pm*
R.K.W., # 70-0-01	9:30 am	11:35 am	1:35 pm	3:00 pm*
Thursday, May 23, 1963				
R.N. McA., # 70-0-07	8:45 am			
W.R.S., # 70-0-08	11:07 am			
C.B.B., # 70-0-06	11:05 am			
T.H.L., # 70-0-09	11:55 am			
R.G.W., # 70-0-10	2:15 pm			
R.K.W., # 70-0-01	-------			

* Physiological monitoring was done during these tests.

ISOMETRIC EXERCISE ROUTINE

1. Positioning:

Press with shoulders into padded cuffs.

Press with heels only against footboard, evenly and low.

Dorsiflex foot: Keep forefoot tilted away from footboard.

Keep lumbar area (low back) flat on table--do not arch back.

Tilt pelvis upward, place hands under buttocks.

Breathe deeply and at regular rate--do not hold breath at any time.

2. Trials:

a. Ten trials, 5 sec. push, 5 sec. relax, with knees flexed to block level, muscles tensed steadily.

b. Look at meter, maintain level that is assigned, constantly for 5 sec.

c. Five trials, 5 sec. push, 5 sec. relax, knee blocks removed, go into full extension at knees and hips. Maintain level steadily.

3. Rounds:

Monday	May 20	1 round, pm
Tuesday	May 21	4 rounds, 2-hour intervals
Wednesday	May 22	4 rounds, 2-hour intervals
Thursday	May 23	1 round before tilt studies

X-RAY DENSITOMETRY STUDIES PROCEDURES

1. Bone densitometry studies were conducted before and after immobilization on May 5,9,19,23, and completed on May 24.

2. X-rays were taken of the os calcis and the third lumbar vertebra according to a standardized technique.

3. These studies were conducted by Dr. Pauline Mack of Texas Woman's University under a separate contract she holds with NASA.

4. The X-ray development facilities of the TIRR were put at Dr. Mack's disposal for checking adequacy of the films taken.

5. Samples of urine were collected and given to Dr. Mack for the purpose of establishing correlation with the bone densitometry studies.

APPENDIX B

COMPREHENSIVE EXPERIMENTAL PROTOCOL

FOURTEEN-DAY IMMOBILIZATION STUDY

Texas Institute for Rehabilitation and Research

Date		Procedure	Responsible
July			
15	8:30 am	BMR - T.G.O., A.C.L.	DC
		X-ray densitometry studies	M
	9:00 am	Breakfast	D
	9:30 am	Ergometry studies - T.G.O., and A.C.L.	DC
	12:30 pm	Lunch	D
	1 pm	Standard admission on 4 selected subjects, D.C. III, R.B., T.G.O., and A.C.L.	AO
		Routine laboratory work on 4 subjects	L
		X-ray densitometry on 2 subjects, D.C. III, and R.B.	M
		ECG on 2 subjects, T.G.O., and R.B.	T
		Routine physicals and history on 4 subjects, T.G.O., A.C.L., D.C. III, and R.B.	CV
	5:30 pm	Dinner	D
	9 pm	Lights out	O
16	8:30 am	BMR - D.C. III, and R.B.	DC
		(Special urine and blood work on R.B.)	L
	8:45 am	Breakfast	D
	10:15 am	Ergometry studies - D.C. III, and R.B.	DC
	10:30 am	5th subject admitted, M.G.O.	AO
		Social Service interview, A.C.L.	MM
		X-ray densitometry on M.G.O.	M
		Routine laboratory work on M.G.O.	L
	12 noon	ECG on A.C.L.	T

Date			Procedure	Responsible
16 - cont.	12:30	pm	Lunch	D
	1	pm	Psychiatric Interviews start	K
	3	pm	Physical and history on M.G.O.	CV
			ECG on D.C. III	T
	4:30	pm	Photography - all subjects	DK
	5:30	pm	Dinner	D
	9	pm	Lights out	O
17	7	am	Start urine collections on 12-hour basis on five subjects	O
	7:15	am	Weight and temperature on all subjects	O
	7:45	am	Carmine dye caps, all subjects for beginning of feces collection	O
	8:30	am	Breakfast (all except R.B.)	D
	9	am	Social Service interview, T.G.O.	MM
	9:25	am	Glucose tolerance test on R.B.	L
	12:45	pm	C.L.B. (6th subject) reported and was admitted	AO
	1	pm	Lunch (all except glucose tolerance subject)	D
			X-ray densitometry on C.L.B.	M
			Routine laboratory on C.L.B.	L
			Social Service interviews continued and completed on 5 subjects	MM
			ECG on C.L.B.	T
			Physical and history on C.L.B.	CV
	5:30	pm	Dinner	D
	7	pm	Finish 12-hour urine collections	S,O
	9	pm	Lights out	O
18	7	am	Start C.L.B. on 12-hour urine collections. Finish 12-hour night collection of urine all other subjects	S,O
	7:30	am	Weight and temperature on all subjects	O
	8	am	Blood volumes	Mc
	8:30	am	Breakfast	D
	9:22	am	Carmine caps for C.L.B.	O
	10	am	C.L.B. to Social Service	MM

Date		Procedure	Responsible
18 - cont.	12:30 pm	Lunch	D
	1 pm	R.B. dismissed from study for medical reason	CV
	2:30 pm	C.L.B. to photography	DK
	3 pm	C.L.B. (Psychiatric interview)	K
	4:15 pm	C.P. admitted to replace R.B.	AO
	4:20 pm	Routine laboratory work on C.P.	L
	4:45 pm	ECG on C.P.	T
	5:30 pm	Dinner	D
	7 pm	Finish 12-hour urine collections	S,O
	8 pm	Fasting begins for glucose tolerance in am	S,O
	8:30 pm	Weight and temperatures on all subjects	O
	9 pm	Lights out	O
19	7 am	Finish 12-hour night collection of urine on 5 subjects	S,O
		Start C.P. on 12-hour collection procedure	S,O
	7:45 am	Temperatures on all subjects	O
	8 am	Blood volumes, LDH	Mc
	8:30 am	Start glucose tolerance test on all subjects	L
	12 noon	Bedside monitoring during glucose tolerance test	T
	1:30 pm	Lunch	D
		Social Service interview for C.P.	MM
		Psychiatric interview for C.P.	K
	5:30 pm	Dinner	D
	7 pm	Finish 12-hour urine collections	S,O
	8 pm	Fasting begins for lipids absorption test on Saturday, July 20,1963	S,O
	9 pm	Lights out	O
20	7 am	Finish 12-hour urine collection on all subjects	S,O
	7:30 am	Weights and temperatures on all subjects	O
	8 am	Blood draw for retic count and LDH	L
	8:30 am	NO breakfast, dietician will provide cream for all subjects	D

Date			Procedure	Responsible
20 - cont.	9	am	Lipid absorption test on all subjects	CV
			Obtain clotted blood at following times: 1 hour, 2 hours, 3 hours, 4 hours	
	12:30	pm	Lunch (provided lipid absorption test is completed)	D
	5:30	pm	Dinner	D
	7	pm	Complete 12-hour urine collection	S,O
	9	pm	Lights out	O
21	7	am	Finish 12-hour urine collection on all subjects	S,O
	7:30	am	Weights and temperatures on all subjects	O
	8	am	Bedside monitoring on all subjects	T
	8:30	am	Breakfast	D
	9	am	X-ray densitometry studies	M
	12:30	pm	Lunch	D
	5:30	pm	Dinner	D
	7	pm	Finish 12-hour urine collection on all subjects	S,O
	9	pm	Lights out	O
22	7	am	Finish 12-hour urine collection on all subjects	S,O
	7:30	am	Weight and temperature on all subjects	O
	7	am	Bedside monitoring	T,O
	8	am	Blood volumes (pre-tilt)	Mc
			Blood draw for additional tests (See blood collection procedure)	L
	8:30	am	Breakfast	D
			X-ray densitometry studies	M
	9	am	Start Tilt Procedures	CV
	NOTE: following tilt: T.G.O., M.G.O., D.C.III, and C.L.B.		Alvar-gradients on 4 subjects	F
			(3-hour pooled urine for MHMA - see urine collection procedure)	L,O
			(Samples of venous blood for 17-OH)	HL

Date			Procedure	Responsible
22 - cont.	12:30	pm	Lunch Continue with tilt	D
	NOTE: All subjects will be given 3 capsules of wood charcoal as markers for fecal collections following tilt			
			All subjects immobilized following tilt procedures	Mc
	5:30	pm	Dinner	D
	7	pm	Finish 12-hour urine collections (minus special collection)	O
			Bedside monitoring	T
	9	pm	Lights out	O
	NOTE: Orderlies on duty after lights out will use subjects' night lights to assist them in making collections of urine and feces. A flashlight has been provided for the orderlies' use in making entries on subjects' intake-output documents.			
23	7	am	Finish 12-hour urine collection on all subjects	S,O
			Bedside monitoring	T
	8	am	Blood volumes LDH	Mc
			Temperatures on all subjects	O
	8:30	am	Breakfast	D
			X-ray densitometry	M
	12:30	am	Lunch	D
	5:30	pm	Dinner	D
	7	pm	Bedside monitoring	T
			Finish 12-hour urine collections on all subjects	O
			Temperatures on all subjects	O
	9	pm	Lights out	O
	11	pm	Orderly change	O
24	7	am	Finish 12-hour urine collections on all subjects	S,O
			Bedside monitoring	T
			Temperatures on all subjects	O

Date			Procedure	Responsible
24 - cont.	8	am	Blood volumes LDH	Mc
	8:30	am	Breakfast	D
			X-ray densitometry studies	M
	12:30	pm	Lunch	D
	2	pm	Bedside monitoring on T.G.O.	T
	5:30	pm	Dinner	D
	7	pm	Finish 12-hour urine collections on all subjects	S,O
			Bedside monitoring	T
			Temperatures on all subjects	T
	NOTE: Special telephone jacks have been installed in the subjects' laboratory to enable them to make a limited number of phone calls in the evening. Each subject will be limited to 15 minutes use of the phone each evening. Phone calls will not be accepted for the subjects at any other time unless they constitute an emergency.			
	9	pm	Lights out	O
	11	pm	Orderly change	
25	7	am	Finish 12-hour urine collection on all subjects	S,O
			Bedside monitoring	T
			Temperatures on all subjects	O
	8	am	Blood volumes	Mc
			Retic. count, LDH	L
	8:30	am	Breakfast	D
			X-ray densitometry studies	M
			Arterial blood pressures on all subjects	W
	12:30	pm	Lunch	D
	5:30	pm	Dinner	
	7	pm	Finish 12-hour urine collections on all subjects	S,O
			Bedside monitoring	T
			Temperatures on all subjects	O
	9	pm	Lights out	
	11	pm	Orderly change	O

Date			Procedure	Responsible
26	7	am	Finish 12-hour urine collections on all subjects	S,O
			Bedside monitoring on all subjects	T
			Temperatures on all subjects	O
	8	am	LDH	
	8:30	am	Breakfast	D
			X-ray densitometry studies	M
	12:30	pm	Lunch	D
	5:30	pm	Dinner	D
	7	pm	Bedside monitoring on all subjects	T
			Finish 12-hour urine collections on all subjects	S,O
			Temperatures on all subjects	O
	9	pm	Lights out	O
	11	pm	Orderly change	O
27	7	am	Finish 12-hour urine collection on all subjects	S,O
			Temperatures on all subjects	O
			Bedside monitoring on all subjects	T
	8:30	am	Breakfast	D
	12:30	pm	Lunch	D
	5:30	pm	Dinner	D
	7	pm	Finish 12-hour urine collections on all subjects	S,O
			Bedside monitoring on all subjects	T
			Temperatures on all subjects	O
	9	pm	Lights out	
	11	pm	Orderly change	O
28	7	am	Finish 12-hour urine collections on all subjects	S,O
			Start urine corticoids collection (7 am to 3 pm)	HL
			Bedside monitoring on all subjects	T
			Temperatures on all subjects	O
	8:30	am	Breakfast	D
	12:30	pm	Lunch	D
	3	pm	Urine corticoids (3 pm to 11 pm)	HL

Date			Procedure	Responsible
28 - cont.	3	pm	Start blood corticoids and LDH	HL
			Start 4-hour bedside monitoring on all subjects	T
	5:30	pm	Dinner	D
	7	pm	Blood corticoids and LDH	HL
			Bedside monitoring on all subjects	T
			Temperatures on all subjects	O
	9	pm	Lights out	O
	11	pm	Urine corticoids (11 pm to 7 am, July 29)	L
			Blood corticoids and LDH	HL
			Bedside monitoring on all subjects	T
			Orderly change	
29	3	am	Blood corticoids and LDH; bedside monitoring	HL, O,T
	7	am	Blood corticoids and LDH	HL
			Urine corticoids (7 am to 3 pm)	L
			Bedside monitoring	T
			Temperatures on all subjects	O
	8:30	am	Breakfast	D
			X-ray densitometry studies	M
	11	am	Blood corticoids and LDH	HL
			Bedside monitoring	T
	12:30	pm	Lunch	D
	3	pm	Urine corticoids (3 pm to 11 pm)	L
			Blood corticoids and LDH	HL
			Bedside monitoring	T
	5:30	pm	Dinner	D
	7	pm	Blood corticoids and LDH	HL
			Bedside monitoring	T
			Temperatures on all subjects	O
	9	pm	Lights out	O
	11	pm	Urine corticoids (11 pm to 7 am, July 30)	L
			Bedside monitoring	T
			Orderly changes	
30	3	am	Bedside monitoring on all subjects	T
	7	am	Finish urine corticoids collection on all subjects	L
			Blood corticoids	HL
			Temperatures on all subjects	O

Date			Procedure	Responsible
30 - cont.	7:15	am	Bedside monitoring on all subjects	T
	8	am	Blood volumes, retic. count, LDH	Mc
	8:30	am	Breakfast	D
	12:30	pm	Lunch	D
	5:30	pm	Dinner	D
	7	pm	Finish 12-hour urine collections on all subjects	S,O
			Bedside monitoring on all subjects	T
			Blood corticoids	HL
			Temperatures on all subjects	O
	9	pm	Lights out	O
	11	pm	Orderly change	O
31	7	am	Blood corticoids	HL
			Finish 12-hour urine collections on all subjects	S,O
			Bedside monitoring on all subjects	T
			Temperatures on all subjects	O
	8:30	am	Breakfast	D
	12:30	pm	Lunch	D
	5:30	pm	Dinner	D
	7	pm	Blood corticoids	HL
			Finish 12-hour urine collections on all subjects	S,O
			Bedside monitoring on all subjects	T
			Temperatures on all subjects	O
	9	pm	Lights out	O
	11	pm	Orderly change	O
August				
1	7	am	Finish 12-hour urine collections on all subjects	S,O
			Bedside monitoring on all subjects	T
			Temperatures on all subjects	O
	7:50	am	Blood volumes	Mc
			LDH	L
			X-ray densitometry studies	M
	8:30	am	Breakfast	D
	12:30	pm	Lunch	D
	5:30	pm	Dinner	D

Date			Procedure	Responsible
1 - cont.	7	pm	Finish 12-hour urine collection on all subjects	S,O
			Temperatures on all subjects	O
	8	pm	Fasting for glucose tolerance on following day: no food or water until notified	
	9	pm	Lights out	O
	11	pm	Orderly change	O
2	7	am	Finish 12-hour urine collection on all subjects	S,O
			Temperatures on all subjects	O
			Bedside monitoring on all subjects	T
	7:30	am	LDH	L
	8:30	am	NO breakfast, special preparation by dietician for glucose tolerance test. Subjects can have water after glucose breakfast	
	12:30	pm	Lunch (upon completion of glucose tolerance test)	D
	5:30	pm	Dinner	D
	7	pm	Finish 12-hour urine collections on all subjects	S,O
			Temperatures on all subjects	O
			Bedside monitoring on all subjects	T
	8	pm	Fasting for all subjects, no food or water until notified	
	9	pm	Lights out	O
	11	pm	Orderly change	O
3	7	am	Finish 12-hour urine collections on all subjects	S,O
			Bedside monitoring on all subjects	T
			Temperatures on all subjects	O
	8	am	LDH	
			Lipid absorption test on all subjects	V,L
	8:30	am	NO breakfast, special preparation by dietician	D
	12:30	pm	Lunch (upon complete of lipid absorption test)	D
	5:30	pm	Dinner	D

Date			Procedure	Responsible
3 - cont.	7	pm	Finish 12-hour urine collections on all subjects	S,O
	9	pm	Lights out	O
	11	pm	Orderly change	O
4	7	am	Finish 12-hour urine collections on all subjects	S,O
			Bedside monitoring on all subjects	T
			Temperatures on all subjects	O
	8:30	am	Breakfast	D
			ECG on all subject	T
	12:30	pm	Lunch	D
	5:30	pm	Dinner	D
	7	pm	Finish 12-hour urine collection on all subjects	S,O
			Bedside monitoring on all subjects	T
			Temperatures on all subjects	O
			A.C.L. , no food from 7 pm, can have small amount of water if necessary.	O
	9	pm	Lights out	O
	11	pm	Orderly change	O
5	6:45	pm	BMR, A.C.L.	T
	7	am	Finish 12-hour urine collection on all subjects	S,O
			Bedside monitoring on all subjects	T
			Temperatures on all subjects	O
	7:15	am	Breakfast	D
	7:30	am	Blood volume	Mc
			Blood drawn for additional tests (See blood collection procedures)	L
	8	am	Start tilt procedures	CV
			NOTE: All subjects to be given 3 carmine dye capsules just prior to tilt. Each subject will be asked to void just prior to tilt and the same procedure will be followed for urine collection as was done on July 22, 1963.	
			All subjects are to be weighed following tilt	

Date			Procedure	Responsible
5 - cont.	8	am	(Samples of venous blood for 17-OH to be taken during tilt	HL
			X-ray densitometry studies following tilt	M
	12:30	pm	Lunch	D
			Continue with tilt	
	NOTE:		Alvar-gradients on A.C.L., T.G.O., M.G.O., D.C.III, C.L.B., and C.P.	T
	5:30	pm	Dinner	
	7	pm	Bedside monitoring on all subjects	T
			Finish 12-hour urine collection (minus special collection)	S,O
			Temperatures on all subjects	O
	8:30	pm	Subjects to report back to lab	O
	9	pm	Lights out	
	NOTE:		Orderly will stay until 10 pm to be sure all subjects are in and assist the physician on call.	
6	7	am	BMR - A.C.L. (2), T.G.O., and D.C.III	T
			Finish 12-hour urine collection on all subjects	S,O
			Weights and temperatures on all subjects	O
	7:50	am	LDH	L
	8:30	am	Breakfast	D
			E r gometry study on: A.C.L., T.G.O., and D.C.III	DC
	12:30	pm	Lunch	D
	5:30	pm	Dinner	D
	7	pm	Finish 12-hour urine collections on all subjects	S,O
			Bedside monitoring on all subjects	T
			Temperatures on all subjects	O
	8:30	pm	Subjects to report back to lab	
	9:00		Lights out	O

Date			Procedure	Responsible
7	7	am	Finish 12-hour urine collections on all subjects	S,O
			Bedside monitoring on all subjects	T
			LDH	L
			Weights and temperatures on all subjects	S,O
	8:30	am	Breakfast	D
	12:30	pm	Lunch	D
			Social Service interview for C.P.	MM
			Social Service interviews continued with other subjects	MM
	5:30	pm	Dinner	D
	7	pm	Finish 12-hour urine collections on all subjects	S,O
			Bedside monitoring on all subjects	T
			Temperatures on all subjects	O
	8:30	pm	Subjects to report to lab	O
	9	pm	Lights out	O
8	7	am	Finish 12-hour urine collections on all subjects	S,O
			Bedside monitoring on all subjects	T
			Weights and temperatures on all subjects	O
	7:50	am	LDH	L
	8:30	am	Breakfast	D
			Social Service interviews continued	MM
	12:30	pm	Lunch	D
	5:30	pm	Dinner	D
	7	pm	Finish 12-hour urine collections on all subjects	S,O
			Bedside monitoring on all subjects	T
			Temperatures on all subjects	O
	8:30	pm	Subjects to report to lab	O
	9	pm	Lights out	O
9	7	am	Finish 12-hour urine collections on all subjects	S,O
			Weights and temperatures on all subjects	O
			Give charcoal capsules to all subjects	O
			Bedside monitoring on all subjects	T

Date		Procedure	Responsible
9 - cont.	7:50 am	Blood volumes LDH	Mc
	8:30 am	Breakfast	D
		X-ray densitometry studies	M
		ALL COLLECTIONS STOP	
	12:30 pm	Lunch	D
	1 pm	5 subjects dismissed, all subjects dismissed on leave of absence to sign out at Main Nursing Station.	

INITIAL INTERVIEW, PHYSICAL EXAMINATION AND HISTORY

1. All prospective candidates for the study must be interviewed by a physician.

2. At the time of the interview, the subjects will be acquainted in general terms with the experimental design, with the purposes of the study and the possible risks involved.

3. Each subject shall be selected on the basis of his age, current health, past medical history and psychological fitness.

4. A complete history shall be taken and a complete physical examination shall be done by the physician prior to accepting the subject for the study.

5. The initial evaluation shall include:

   a. Statement of present physical condition
   b. Statement of current psychological fitness
   c. A detailed past medical history
   d. A review of systems
   e. A detailed family history
   f. A detailed statement regarding current habits (eating, smoking, drinking, sleeping, exercise, etc.)

6. The physical examination shall be complete and it shall include an examination of:

   a. General appearance, skin, lymphatic system, head, eyes-ears-nose and throat, neck, spine, chest (lungs and heart), abdomen, genitalia, extremities, and neurological. Chest X-rays will be done on each subject.

7. An evaluation of the psychological condition of the subject shall be made by a consultant psychiatrist.

8. An evaluation of the sociological conditions surrounding the subject shall be done by the medical social worker.

9. Each subject shall sign the proper forms and authorizations of release and relinquishing responsibility prior to active participation in the study.

10. Each subject will be admitted to TIRR through routine procedures for the admittance of all patients. Standard admitting forms will be used.

FOOD ANALYSIS PROCEDURES AND PROTOCOLS

All subjects were started on special diets on July 16, 1963, at 8:30 am for the first period of this study. All subjects were started on special diets on August 15, 1963, at 8:30 am for the second period of this study.

During the pre-immobilization and post-immobilization phases of each period the subjects were given special diets compiled and prepared in the TIRR kitchen by the dietician assigned to the study. During the periods of immobilization the subjects were given special diets prepared and pre-analyzed by NASA.

1. Subjects shall be on identical carefully controlled diets, shall be required to eat ALL food served, if possible, and shall take no additional food other than that which is served to them in the Immobilization Study Unit.

2. All meals during pre-immobilization and post-immobilization periods prepared at TIRR shall be duplicated and a tray for each meal taken to the laboratory for food analysis. The NASA diet was pre-analyzed.

3. Servings from lunch, dinner and breakfast (following morning) shall be pooled to represent diet for each 24-hour period.

4. The weight of the food shall be recorded and the food shall be analyzed for:
   a. Calcium b. Phosphates c. Nitrogen
   (NASA food not included, was not analyzed for phosphates.)

5. Food Analysis Source Document shall be filled out for each day on each subject by the dietician.

6. The diets for the two study periods contained 2400 calories per day, 1 gm.of calcium and 100 gms. of protein with a low residue.

NUTRITIONAL INTAKE PROTOCOL

1. Each subject shall be on a special diet containing a predetermined amount of calories, minerals and residue.

2. Liquids taken with meals shall be included in the tray prepared for laboratory analysis. Between meals subjects may have fluid as long as distilled water only is consumed or used in the preparation of coffee or tea.

INTAKE AND OUTPUT PROCEDURES

A. INTAKE PROTOCOL

1. All food and liquid intake for each subject shall be recorded in the special source documents.

2. The amount of liquid taken shall be measured exactly. In order to facilitate this measurement, cups measuring eight (8) ounces will be available and when a subject asks for a drink of water he shall be offered a full cup containing eight (8) ounces. Whatever amount is left after drinking shall be measured exactly in order to compute the amount taken.

3. Each subject shall be asked to eat all food contained on the tray offered to him at each meal. All fluid offered with meals shall be taken in by all subjects.

4. In the event that a subject is unable to ingest all the food or liquid offered on his tray, the amounts left over shall be put back on the tray and sent to the laboratory for measurement and analysis.

B. OUTPUT PROTOCOL

1. Solid and liquid output of each subject shall be collected according to specifications given in the protocols for urine collection and also for fecal collections.

2. If the subject perspires during the period of immobilization, a statement regarding the amount of perspiration shall be included in the source documents of clinical observations.

3. A rating will be made of the degree of perspiration according to the following scale: a. trace, b. fair amount, c. moderate amount, d. large amount, e. profuse.

4. If the subject vomits during the period of study, the attending physician shall be notified immediately. The whole amount of vomitus shall be collected if possible and sent to the laboratory for measurement and analysis.

5. The total amount of blood collected on each subject for blood chemical analysis shall be entered in the intake and output record.

FECAL COLLECTION PROCEDURES

July 15, 1963 - August 9, 1963

1. Give marker (3 carmine capsules) just before breakfast on Wednesday, July 17, 1963.

2. Collect every stool in a separate jar from the time the marker first appears. (These jars, pre-weighed will be supplied by the laboratory.) Each jar will have a number. The source document will be sent to the laboratory by the orderly with the jar for each stool and the source document will bear the same number in the left top corner in red pencil which will correspond to the number on the jar.

   On the source document the orderly will fill in: Date and time.

3. Give marker again (3 wood charcoal capsules) just after tilt on Monday, July 22,1963, at the beginning of immobilization period.

4. Give third marker (3 carmine capsules) just before tilt on Monday, August 5,1963. (End of immobilization period)

5. Give fourth marker (3 wood charcoal capsules) just before breakfast on Friday, August 9, 1963.

6. Subjects are all to take feces collecting containers home with them and shall continue to collect feces during this time until the appearance of the wood charcoal. Each jar shall be returned to TIRR as soon as possible. It must be refrigerated if not returned within four hours.

URINE HANDLING PROCEDURES

These procedures were followed for both phases of the Immobilization study.

1. All urine samples shall be pooled for a 12-hour period (7 am - 7 pm) of one day and (7 pm - 7 am) of the following day until specifically indicated otherwise.
2. Urine shall be collected in two separate jars, the clear jar will be for the daytime collection and an amber jar will be used for the night collections.
3. Urine shall be stored in the refrigerator until taken to the laboratory.
4. The pooled urine samples of whatever period shall be utilized for various chemical determinations. However, certain information and procedures are required for each voiding.
5. During immobilization, the following shall be recorded on the Intake-Output documents for EACH VOIDING:
   a. Time.
   b. Measure and record specific gravity (RETURN the sample to the bottle after this measurement is made).
   c. Measure and record total volume of each voiding.
   d. Test urine sample for sugar using Clinistix provided: if sample is positive for a trace amount of sugar, notify the physician on call and he will order a blood sugar test.
   e. Put entire sample in container for the period of pooling.
6. In the event the subject voids while he is absent from the TIRR during the pre-immobilization and post-immobilization observation periods, Step 5 may be carried out after the subject returns to the Institute.
7. To start the pool of urine, proceed as follows:
   a. Have subject urinate and discard sample at the time assigned.
   b. For each and every voiding between this time and the next indicated period, save all urine and test according to instructions.
   c. At the end of each 12-hour period, have subject void (whether he thinks he has to or not) and put into the bottle for that period.
   d. The urine from successive voidings is put into the next 12-hour period bottle.
8. Subjects shall be instructed to empty their bladder (and keep sample) prior to having a bowel movement to prevent mixing of urine and feces.
9. At the end of the period of collection, the untreated, cooled urine shall be taken to the laboratory in the properly labeled containers for processing.

URINE COLLECTION PROCEDURES

Date	Time	Test
15 - 16	Routine urinalysis on admission	2
17	7 am - Start collection for 12-hour pool 7 am to 7 pm - Repeat same for the next 12 hours, 7 pm - 7 am the following morning. The 24-hour pool is considered ended at 7 am on July	On 12-hour pool, 4,6,7
17 - 18	18,1963	On 24-hour pool, 1
18	7 am to 7 pm	
18 - 19	7 pm to 7 am	As above
19	7 am to 7 pm	
19 - 20	7 pm to 7 am	As above
20	7 am to 7 pm	
20 - 21	7 pm to 7 am	As above
21	7 am to 7 pm	
21 - 22	7 pm to 7 am	As above
22	Start of tilt procedures	
	7 am - Collect until the beginning of tilt and put in bottle for testing as above.	
	NOTE: Each subject must void before being placed on tilt table	
	Collect from start of tilt to 3 hours after the beginning tilt procedure. Mark bottle for this collection period	

CODE FOR TESTS

1. Ca, P, N, and Creatinine
2. Routine and microscopic
4. Na, K
6. 17-OH steroids
7. MHMA

Date	Time	Test
	with subject's name and number and the time of the beginning of the tilt procedure, and the time of the end of the 3-hour period	4,6,7
	Collect from the end of the above period up to 7 pm and place in separate bottle	4,6,7
22 - 23	7 pm to 7 am	4,6,7, & 1 on 24-hourpool
23	7 am to 7 pm	
23 - 24	7 pm to 7 am	As on July 17 - 18
24	7 am to 7 pm	
24 - 25	7 pm to 7 am	As on July 17 - 18
25	7 am to 7 pm	
25 - 26	7 pm to 7 am	As on July 17 - 18
26	7 am to 7 pm	
26 - 27	7 pm to 7 am	As on July 17 - 18
27	7 am to 7 pm	
27 - 28	7 pm to 7 am	As on July 17 - 18
28	7 am to 3 pm	4,6,7
	3 pm to 11 pm	4,6,7
28 - 29	11pm to 7 am	4,6,7 & 1 on 24-hour pool
	NOTE: orderlies will use small bottles and mark subject's name, number and time	
29	7 am to 3 pm	4,6,7
	3 pm to 11 pm	4,6,7
29 - 30	11 pm to 7am	4,6,7 & 1 on 24-hour pool
	NOTE: same as above	
30	7 am to 7 pm	
30 - 31	7 pm to 7 am	As on July 17 - 18

Date	Time	Test
31	7 am to 7 pm	
31 - August 1	7 pm to 7 am	As on July 17 - 18
August		
1	7 am to 7 pm	
1 - 2	7 pm to 7 am	As on July 17 - 18
2	7 am to 7 pm	
2 - 3	7 pm to 7 am	As on July 17 - 18
3	7 am to 7 pm	
3 - 4	7 pm to 7 am	As on July 17 - 18
4	7 am to 7 pm	
4 - 5	7 pm to 7 am	As on July 17 - 18
5	Start of tilt procedures	
	7 am - Collect until the beginning of tilt and put in bottle for testing as above.	
	NOTE: Each subject must void before being placed on tilt table.	
	Collect from start of tilt to 3 hours after the beginning of tilt procedure. Mark bottle for this collection period with subject's name and number and the time of the beginning of the tilt procedure, and the time of the end of the 3-hour period.	4,6,7
	Collect from the end of the above period up to 7 pm and place in separate bottle	4,6,7
5 - 6	7 pm to 7 am	4,6,7 & 1 on 24-hour pool

Date	Time	Test
6	7 am to 7 pm	
6 - 7	7 pm to 7 am	As on July 17 - 18
7	7 am to 7 pm	
7 - 8	7 pm to 7 am	As on July 17 - 18
8	7 am to 7 pm	
8 - 9	7 pm to 7 am	As on July 17 - 18
9	All collections stop.	

BLOOD COLLECTION PROCEDURES

CODE	
Blood Tests	**Blood Bottles**
a. Calcium	4. 4 cc. (Clotted)
b. Phosphorus	5. 3 cc. Oxalate
c. Alkaline phosphatase	7. 5 cc. (Clotted)
l. Serology	8. 10 cc. (Clotted)
m. 17-OH corticoids	9. 4 cc. Oxalate
n. Blood volume	10. Finger
o. Protein electrophoresis	
q. LDH	
r. Total protein	
s. CVC	
t. Reticulocyte count	
u. Glucose tolerance	
v. Lipid absorption	

Date	Time	Test	Blood to be Drawn	Comments
July				
15 - 16	on admiss.	l,s,t	10	
18	7:50 am	n	5	Draw and inject isotope
	8 am	n	5	Draw from opposite arm
19	7:50 am	n	5	Fasting, draw and inject isotope
	8 am	n,u,q	5,9,4	Draw from opposite arm and give CHO load
	8:30 am	u	9	
	9 am	u	9	
	10 am	u	9	
	11 am	u	9	
20	8 am	t,v,q	5,7	Fasting and give lipid load
	9 am	v	7	
	10 am	v	7	
	11 am	v	7	
	12 noon	v	7	

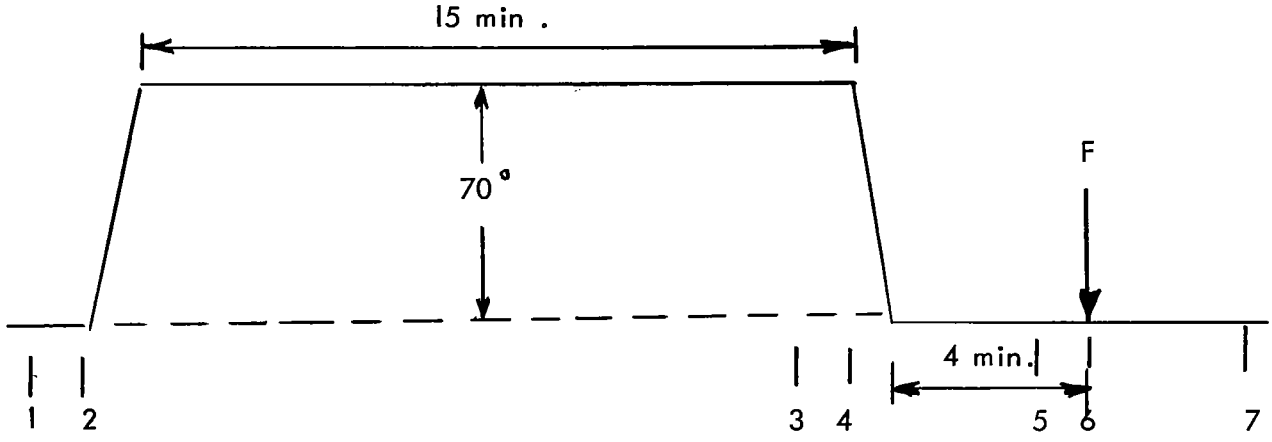
Date	Time	Test	Blood to be Drawn	Comments
22	7:05 am	n	5	Draw and inject isotope
	8 am	n,a,b,c,o,r,s,t	5,9,8	Draw from opposite arm
	During tilt	m	9	From saphenous vein
	After tilt	n	9	Draw and inject isotope
	10 min. later	n	9	Draw from opposite arm
23	7:50 am	n	5	Draw and inject isotope
	8 am	n,q	5,4	Draw from opposite arm
24	7:50 am	n	5	Draw and inject isotope
	8 am	n,q	5,4	Draw from opposite arm
25	7:50 am	n	5	Draw and inject isotope
	8 am	n,q,t	5,4,9	Draw from opposite arm
26	7:50 am	n	5	Draw and inject isotope
	8 am	n,q	5,4	Draw from opposite arm
28	3 pm	m,q	9,4	Draw through intracath
	7 pm	m,q	9,4	Draw through intracath
	11 pm	m,q	9,4	Draw through intracath
29	3 am	m,q	9,4	Draw through intracath
	7 am	m,q	9,4	Draw through intracath
	11 am	m,q	9,4	Draw through intracath
	3 pm	m,q	9,4	Draw through intracath
	7 pm	m,q	9,4	Draw through intracath
30	7:50 am	n	5	Draw and inject isotope
	8 am	n,q,t	5,4,9	Draw from opposite arm
August				
1	7:50 am	n	5	Draw and inject isotope
	8 am	n,q,t	5,4,9	Draw from opposite arm
2	8	u,q	9,4	Fasting, give CHO load
	8:30 am	u	9	
	9 am	u	9	
	10 am	u	9	
	11 am	u	9	

Date	Time	Test	Blood to be Drawn	Comments
3	8 am	v,q	7	Fasting and give lipid load
	9 am	v	7	
	10 am	v	7	
	11 am	v	7	
	12 noon	v	7	
5	7:50 am	n	5	Draw and inject isotope
	8 am	n,q,a,b,c,o,r,s,t	5,9,8	Draw from opposite arm
	During tilt	m	9	From saphenous vein
	After tilt	n	9	Draw and inject isotope
	10 min.	n	9	Draw from opposite arm
6	8 am	q	4	
7	8 am	q	4	
8	8 am	q	4	
9	7:50 am	n	5	Draw and inject isotope
	8 am	n,q,a,b,c,o,r,s,t	5,9,8	Draw from opposite arm

PASSIVE TILT TESTING

Passive tilt testing will be done on each subject according to the attached schedule.

The procedure for the passive tilt testing will be done according to the graphic representation below.



CODE OF SITUATION

F Flack test
1 Steady state supine position 0°
2 Beginning of tilt to 70°
3 Steady state at 70°
4 Beginning of tilt down to 0°
5 Steady state at 0° after tilt and before Flack
6 Beginning of Flack test at 0°
7 Steady state 0° after tilt and after Flack

PREPARATION FOR TILT TESTING

(With the indicated exceptions, the preparation and procedure for tilt testing were the same for the two phases of the immobilization study.)

DATE: July 22, August 5, August 19, and September 2, 1963

Time (Approximate)	Subject No.	Phase I		Phase II	
8 am	1	A.C.L.	70-0-11	A.C.L.	70-0-11
9:30 am	2	T.G.O.	70-0-12	M.G.O.	70-0-13
11 am	3	M.G.O.	70-0-13	D.C. III	70-0-14
1 pm	4	D.C. III	70-0-14	C.L.B.	70-0-16
2:30 pm	5	C.L.B.	70-0-16	C.P.	70-0-17
4 pm	6	C.P.	70-0-17	A.C.I.	70-0-18

INSTRUCTIONS

1. One-half hour prior to tilt, each subject must have his own electrode harness applied (or checked).

2. An intra-arterial needle must be inserted.

3. An intracath must be inserted in the saphenous vein.

4. The subject must void before being placed on the tilt table.

5. All the urine collected up to three hours from the onset of the tilt procedure must be collected and analyzed for MHMA, Na, and K.

6. Blood volume measurements will be made before and after tilt unless indicated otherwise on the Master Protocol.

7. Samples of venous blood will be collected at several points during tilt for measurements of corticosteroids.

8. Throughout the passive tilt test the electrocardiogram, the pneumogram, the carotid pulse, the radial pulse, the phonocardiogram, the intra-arterial pressure and Korotkoff sounds in the brachial artery during the intermittent inflation of a cuff must be monitored. During the Flack test, the pressure in the airway of the subject must be recorded also.

NOTE: * Modified tilt procedures were done on August 14,1963, September 6,1963, and on one subject on September 9,1963 and September 12,1963 (C.P. - 70-0-17). One subject was tilted on September 1,1963, C.L.B. - 70-0-16,and released because of family emergency.

---

* Without direct intra-arterial blood pressure.

MONITORING PROCEDURES

A. BEDSIDE MONITORING

1. Each subject shall have chronically applied electrodes for recording of the electrocardiogram and pneumogram.

2. Pick-ups for recording other physiological variables will be attached to each subject prior to each period of recording, depending on the experimental design.

3. The electrodes and pick-ups shall be connected to the movable cabinet and from there they will be transmitted by connecting cable to a console where the variables will be displayed on an oscilloscope and permanently recorded.

4. The duration of the recordings and the time frequency of the recordings will vary according to each phase of the study and the experimental design.

5. Information pertaining to the subject being monitored at the time will be properly coded on magnetic tape.

B. PHYSIOLOGICAL MONITORING DURING THE FIRST PERIOD OF IMMOBILIZATION (July 15,1963 - August 9, 1963)

1. The following physiological variables must be monitored over a period of three to five minutes: electrocardiogram, phonocardiogram, carotid pulse, radial pulse, pneumogram and Korotkoff sounds at the brachial artery during intermittent cuff inflation. The date, time, and the subject's identification number must be coded in a separate channel of the monitor. The subject must be lying in bed during the period of monitoring.

2. The first monitoring must take place at 7 am on July 19,1963,and it must be repeated every 12 hours until the last monitoring at 7 pm on August 8, 1963.

3. On July 28, 1963, physiological monitoring of each subject will be carried out at: 7 am, 3 pm, 7 pm, 11pm. On July 29,1963, records will be obtained at: 3 am, 7 am, 11 am, 3 pm,and 7 pm.

4. All efforts to not waken the patient during the night periods of monitoring should be made. In order to secure this, the BP pump will not be turned on for recording the blood pressure.

GLUCOSE TOLERANCE AND LIPID ABSORPTION

PROCEDURE

1. GTT and LTT should not be run on the same day.

2. Glucose tolerance test--with patient on good carbohydrate intake for several days prior to test, give patient 100 gram carbohydrate breakfast from dietary department (or may give orally 100 grams of glucose in water). Patient should be fasting for 12 hours prior to test. Take the following blood samples: a. fasting, b. 30 minutes, c. 2 hours, d. 3 hours, and e. 4 hours.

The glucose tolerance and lipid absorption tests were done during the first phase of this study only.

ORDERLIES' DUTY SCHEDULE

NOTE: If at any time during the course of this study an orderly should note what he considers to be extreme behavior or unusual activity on the part of any subject, DO NOT attempt to handle the situation alone; call the "physician on call". If a physician is present in the room at the time, quietly call the matter to his attention.

1. 7 am Lights on in subject lab.

2. Check for notes and protocol for the day.

3. 7 am Subjects must void at 7 am for completion of 7 pm - 7 am collection. Follow procedures for testing and measuring and adding to collection jars.

4. am Check jars for fecal collections and two jars for up-coming periods of urine collections unless special collection procedures are indicated on the protocols.

5. Urine collections should be taken to the laboratory each am upon completion of the 7 am voiding.

6. Orderlies will assist with bedside monitoring on days indicated.

7. Obtain clean scrub suits each day for the subjects and during the period of immobilization assist with personal care.

8. Record all blood withdrawn from the subjects in each 12-hour period. If the information is not proffered by the individual drawing blood, make a polite request for the amount of blood drawn.

9. Weight and temperatures as indicated on protocol.

10. Intake-Output sheets (previously explained -- measure all water given to subjects and make proper entry. Record intake with meals.) Each orderly will initial all entries he makes on Protocol sheets as well as on Intake-Output and Bedside Observations documents.

11. Bedside Observation Notes: Make in spare time unless unusual occurrence, such as, profuse sweating, vomiting, extreme depression or anxiety or medication, etc. Make notation with specific time and in the event of medication be sure information is recorded on "physician's orders" document.

12. On days of tilt studies, all orderlies may be required to work overtime or double-up on duty. Please make plans accordingly. Orderlies will complete "pulse wave velocity" documents on monitoring days as previously instructed by Dr. Vallbona.

13. "Bone Densitometry Studies" conducted during the immobilization period will require the orderlies' assistance. Dr. Pauline B. Mack from T.W.U. is here under separate contract from NASA to conduct these studies. Your full cooperation is expected to assist Dr. Mack at any time.

14. Fasting periods are indicated on the protocol. Please insist that the subjects observe these regulations.

15. Mary Walters, dietician for these studies, will instruct and assist the orderlies in making computations on fluid intake with meals.

    a. Sugar given with any meal must be consumed with the meal by subjects.
    b. Salt and pepper can be utilized on preference basis.
    c. Coffee or tea can be served interchangeably and the amount of fluid recorded for each meal.

16. During the immobilization period, the 11 pm - 7 am shift will be covered by the TIRR orderlies through the office of the Director of Nursing. A schedule of the orderlies will be furnished and posted in the subjects' lab.

Your cooperation, evaluation and accuracy will be appreciated. Please feel free to ask questions. If you make a mistake in your calculations or entries, please indicate or call it to the attention of the physician in charge.

Date			Procedure	Responsible
August				
14	7:45	am	X-ray densitometry studies on all subjects	M
	8	am	Start "Modified Tilt Procedures" (without direct intra-arterial blood pressures)	CV
	9:30	am	Ergometry studies on A.C.L., T.G.O., and D.C.III	T
	12:30	pm	Lunch After evaluation, return 5 subjects from L.O.A. dismissal and discharge one subject, T.G.O., unable to participate in second period of study because of school commitment.	D
	3	pm	Interval history and physical	CV
	5:30	pm	Dinner Subjects are to spend night at TIRR	D
	9	pm	Lights out	O
15	7	am	3 carmine dye capsules for all five subjects	O
			Start 12-hour urine collections on all five subjects	S,O
			Weights and temperatures on all five subjects	S,O
	7:30	am	Admit one new subject, A.C.I. Routine laboratory work and admitting office at 9 am	
	8	am	CBC, retic count and routine urinalysis on all subjects	L
			Routine chest X-rays on all subjects	R
	8:30	am	Breakfast (start special diet)	D
	9	am	Ergometry study on M.G.O.	T
	12:30	pm	Lunch	
	1	pm	ECG on A.C.I.	T
	1:30	pm	Social Service interview on A.C.I.	MM
	5:30	pm	Dinner	D

Date			Procedure	Responsible
15 - cont.	7	pm	Finish 12-hour urine collection on 5 subjects	S,O
			Bedside monitoring on all subjects	T
	9	pm	Lights off	O
	11	pm	T.V. off	O
	NOTE:		Fasting for three subjects to have BMR and ergometry in morning	
16	7	am	Finish 12-hour urine collections on all subjects	S,O
			BMR on A.C.I. only.	T
	7:30	am	Weight and temperatures on all subjects	O
	8:30	am	Breakfast	D
	10	am	Blood volumes on all subjects	Mc
			LDH	L
	10:30	am	Ergometry studies on A.C.I., C.L.B., and C.P.	T
	12:30	pm	Lunch	D
	5:30	pm	Dinner	D
	7	pm	Finish 12-hour urine collections on all subjects	S,O
	9	pm	Lights out	O
	11	pm	T.V. off	O
17	7	am	Finish 12-hour urine collection on all subjects	S,O
			Bedside monitoring on all subjects	T
			Weight and temperatures on all subjects	S,O
	8:30	am	Breakfast	D
	12:30	pm	Lunch	D
	5:30	pm	Dinner	D
	7	pm	Finish 12-hour urine collection on all subjects	S,O
			Bedside monitoring on all subjects	T
	9	pm	Lights out	O
	11	pm	T.V. off	O

Date			Procedure	Responsible
18	7	am	Finish 12-hour urine collections on all subjects	S,O
			Weight and temperatures on all subjects	O
	8:30	am	Breakfast	D
	10	am	Exercise program rehearsal	B
	12:30	pm	Lunch	D
	1:30	pm	Exercise program rehearsal continues	B
	5:30	pm	Dinner	D
	7	pm	Finish 12-hour urine collections on all subjects	S,O
	9	pm	Lights out	O
	11	pm	T.V. off	O
19	7	am	Finish 12-hour urine collections on all subjects	S,O
			Weight and temperatures on all subjects	O
	7:30	pm	Breakfast	D
			X-ray densitometry studies on all subjects	M
			Blood volumes	Mc
			Blood draw for additional tests (See blood collection procedures)	L
	8	am	Start tilt procedures	CV
	NOTE: Orderlies will assist with tilt and be sure each subject voids just prior to being placed on tilt table.			
			Alvar-gradient following tilt on Irwin only	T
			3 carmine dye capsules for all subjects following tilt procedure	O
			All subjects immobilized following tilt procedure	
	12:30	pm	Lunch	D
			Continue with tilt	CV
	5:30	pm	Dinner	D

Date			Procedure	Responsible
19 - cont.	7	pm	Finish 12-hour urine collections on all subjects	S,O
	9	pm	Lights out	O
	11	pm	T.V. off	O
			Orderly change	
20	7	am	Finish 12-hour urine collections on all subjects.	S,O
			Temperatures on all subjects	O
			X-ray densitometry studies on all subjects	M
	8	am	Blood volumes	Mc
			LDH	L
	8:30	am	Breakfast	D
	9	am	Exercise program begins with bedside monitoring on all subjects	T
	12:30	pm	Lunch	D
	1:30	pm	Exercise continued	T
	5:30	pm	Dinner	D
	7	pm	Finish 12-hour urine collections on all subjects	S,O
			Bedside monitoring on all subjects	T
			Temperatures on all subjects	O
	9	pm	Lights out	O
	11	pm	T.V. off	O
			Orderly change	
21	7	am	Finish 12-hour urine collections on all subjects	S,O
			Temperatures on all subjects	O
			X-ray densitometry studies on all subjects	M
	8	am	Blood volumes	Mc
			LDH	L
	8:30	am	Breakfast	D
	9	am	Exercise program	T
	12:30	pm	Lunch	D
	1:30	pm	Exercise program	T
	5:30	pm	Dinner	D
	7	pm	Finish 12-hour urine collections on all subjects	S,O
			Temperatures on all subjects	O

Date			Procedure	Responsible
21 - cont.	9	pm	Lights out	O
	11	pm	T.V. off	O
			Orderly change	
22	7	am	Finish 12-hour urine collections on all subjects	S,O
			Temperatures on all subjects	O
			Bedside monitoring on all subjects	T
			X-ray densitometry studies on all subjects	M
	8:30	am	Breakfast	D
	9	am	Exercise program	T
	12:30	pm	Lunch	D
	1:30	pm	Exercise program continued	T
	5:30	pm	Dinner	D
	7	pm	Finish 12-hour urine collections on all subjects	S,O
			Bedside monitoring on all subjects	T
			Temperatures on all subjects	O
	9	pm	Lights out	O
	11	pm	T.V. off	O
			Orderly change	
23	7	am	Finish 12-hour urine collections on all subjects	S,O
			Temperatures on all subjects	O
	8	am	Blood volumes	Mc
			LDH	L
			X-ray densitometry studies on all subjects	M
	8:30	am	Breakfast	D
	9	am	Exercise program	T
	12:30	pm	Lunch	D
	1:30	pm	Exercise program continued	T
	5:30	pm	Dinner	D
	7	pm	Finish 12-hour urine collections on all subjects	S,O
			Temperatures on all subjects	O
	9	pm	Lights out	O
	11	pm	T.V. off	O
			Orderly change	

Date			Procedure	Responsible
24	7	am	Finish 12-hour urine collections on all subjects	S,O
			Temperatures on all subjects	O
	8:30	am	Breakfast	D
	9	am	Exercise program	T
	12:30	pm	Lunch	D
	1:30	pm	Exercise program continued	T
	5:30	pm	Dinner	D
	7	pm	Finish 12-hour urine collections on all subjects	S,O
			Temperatures on all subjects	O
	9	pm	Lights out	O
	11	pm	T.V. off	O
			Orderly change	
25	7	am	Finish 12-hour urine collections on all subjects	S,O
			Temperatures on all subjects	O
			X-ray densitometry studies on all subjects	M
	8:30	am	Breakfast	D
	9	am	Exercise program	T
	12:30	pm	Lunch	D
	1:30	pm	Exercise continued during afternoon	T
	5:30	pm	Dinner	D
	7	pm	Finish 12-hour urine collections on all subjects	S,O
			Temperatures on all subjects	O
	9	pm	Lights out	O
	11	pm	T.V. off	O
			Orderly change	
26	7	am	Finish 12-hour urine collections on all subjects	S,O
			Temperatures on all subjects	O
	8:30	am	Breakfast	D
	9	am	Exercise with bedside monitoring	T
	12:30	pm	Lunch	D
	1:30	pm	Exercise program continued	T
	5:30	pm	Dinner	D
	7	pm	Finish 12-hour urine collections on all subjects	S,O
			Temperatures on all subjects	O

Date			Procedure	Responsible
26 - cont.	9	pm	Lights out	O
	11	pm	T.V. off	O
			Orderly change	O
27	7	am	Finish 12-hour urine collections on all subjects	S,O
			Temperatures on all subjects	O
			Bedside monitoring	T
	8	am	Blood volume	Mc
			LDH	L
			X-ray densitometry studies on all subjects	M
	8:30	am	Breakfast	D
	9	am	Exercise program	T
	12:30	pm	Lunch	D
	1:30	pm	Exercise program continued	T
	5:30	pm	Dinner	D
	7	pm	Finish 12-hour urine collections on all subjects	S,O
			Bedside monitoring on all subjects	T
			Temperatures on all subjects	O
	9	pm	Lights out	O
	11	pm	T.V. off	O
			Orderly change	O
28	7	am	Finish 12-hour urine collections on all subjects	S,O
			Temperatures on all subjects	O
			Bedside monitoring on all subjects	T
	8:30	am	Breakfast	D
	NOTE: NASA food was discontinued on this date and subjects were started on special diets from the kitchen of TIRR as calculated by the dietician for the study			
	9	am	Exercise program	T
	12:30	pm	Lunch	D
	1:30	pm	Exercise continued during afternoon	T
	5:30	pm	Dinner	D

Date			Procedure	Responsible
28 - cont.	6	pm	Group interview with Mrs. Mitchell from Social Service	
	7	pm	Finish 12-hour urine collections on all subjects	S,O
			Temperatures on all subjects	O
			Bedside monitoring on all subjects	T
	9	pm	Lights out	O
	11	pm	T.V. off	O
			Orderly change	
29	7	am	Finish 12-hour urine collections on all subjects	S,O
			Temperatures on all subjects	O
			Bedside monitoring on all subjects	T
	8	am	X-ray densitometry studies on all subjects	M
	8:30	am	Breakfast	D
	9	am	Exercise program	T
	12:30	pm	Lunch	D
	1:30	pm	Exercise program continued	T
	5:30	pm	Dinner	D
	7	pm	Finish 12-hour urine collections on all subjects	S,O
			Temperatures on all subjects	O
			Bedside monitoring on all subjects	T
	9	pm	Lights out	O
	11	pm	T.V. off	O
			Orderly change	
30	7	am	Finish 12-hour urine collections on all subjects	S,O
			Temperatures on all subjects	O
			Bedside monitoring on all subjects	T
	8:30	am	Breakfast	D
	9	am	Exercise program	T
	12:30	pm	Lunch	D
	1:30	pm	Exercise program continued	T
	5:30	pm	Dinner	D
	7	pm	Finish 12-hour urine collections on all subjects	S,O
			Temperatures on all subjects	O
			Bedside monitoring on all subjects	T

Date			Procedure	Responsible
30 - cont.	9	pm	Lights out	O
	11	pm	T.V. off	O
			Orderly change	
31	7	am	Finish 12-hour urine collections on all subjects	S,O
			Temperatures on all subjects	O
	8	am	X-ray densitometry studies on all subjects	M
	8:30	am	Breakfast	D
			ECG on all subjects	T
	9	am	Exercise program	T
	12:30	pm	Lunch	D
	1:30	pm	Exercise program continued	T
	5:30	pm	Dinner	D
	7	pm	Finish 12-hour urine collections on all subjects	S,O
			Temperatures on all subjects	O
			Bedside monitoring on all subjects	T
	9	pm	Lights out	O
	11	pm	T.V. off	O
			Orderly change	
September				
1	7	am	Finish 12-hour urine collections on all subjects	S,O
			Temperatures on all subjects	O
			Bedside monitoring on all subjects	T
			Tilt procedure on C.L.B. (due to emergency in family, C.L.B. was tilted and released to return if possible on September 6, 1963.)	CV
			Alvar-gradient on C.L.B. following tilt	T
	8:30	am	Breakfast	D
	9	am	Exercise program	T
	12:30	pm	Lunch	D
	1:30	pm	Exercise continued during afternoon	T
	5:30	pm	Dinner	D

Date			Procedure	Responsible
1 - cont.	7	pm	Finish 12-hour urine collection on five subjects	S,O
			Temperature on all subjects	O
			Bedside monitoring on all subjects	T
	9	pm	Lights out	O
	11	pm	T.V. off	O
			Orderly change	
2	7	am	Finish 12-hour urine collections on all subjects	S,O
			Temperatures on all subjects	O
			Bedside monitoring on all subjects	T
	7:15	am	Blood volumes	Mc
			LDH and blood draw for additional tests (See blood collection procedures)	L
			X-ray densitometry studies on all subjects	M
	7:30	am	Breakfast	D
	8	am	Start tilt procedures	CV
	NOTE: Orderlies will assist with tilt and be sure each subject voids just prior to being placed on tilt table			
			3 carmine dye capsules for each subject just before tilt	O
			Weights on all subjects immediately following tilt	O
	12:30	pm	Lunch	D
			Continue with tilt	
			C.P. was discharged following tilt due to his teaching schedule	
	5:30	pm	Dinner	D
	7	pm	Finish 12-hour urine collections on all subjects	S,O
			Temperatures on all subjects	O
	9	pm	Lights out	O
	11	pm	T.V. off	O
			Orderly change	
	NOTE: Fasting after 8 pm for A.C.L., , M.G.O., and D.C.III			

Date			Procedure	Responsible
3	7	am	Finish 12-hour urine collections on all subjects	S,O
			Weights and temperatures on all subjects	O
			Bedside monitoring on all subjects	T
	7:30	am	BMR on 3 subjects, A.C.L., M.G.O., and D.C.III	T
	8:30	am	Breakfast	D
			Ergometry studies on 3 subjects, A.C.L., M.G.O., and D.C.III	T
	12:30	pm	Lunch	D
	5:30	pm	Dinner	D
	7	pm	Finish 12-hour urine collections on all subjects	S,O
			Temperatures on all subjects	O
			Fasting after 8 pm for A.C.I.	
	9	pm	Lights out	O
	11	pm	T.V. off	O
			Orderly change	
4	7	am	Finish 12-hour urine collections on all subjects	S,O
			Weights and temperatures on all subjects	O
			Bedside monitoring on all subjects	T
	7:30	am	BMR on A.C.I.	T
			X-ray densitometry studies on all subjects	M
	8:30	am	Breakfast	D
			Ergometry studies on A.C.I., and C.P.	T
	12:30	pm	Lunch	D
	5:30	pm	Dinner	D
	7	pm	Finish 12-hour urine collections on all subjects	S,O
			Temperatures on all subjects	O
	9	pm	Lights out	O
	11	pm	T.V. off	O
			Orderly change	

Date			Procedures	Responsible
5	7	am	Finish 12-hour urine collections on all subjects	S,O
			Weights and temperatures on all subjects	O
			Bedside monitoring on all subjects	T
			Blood volumes	Mc
			LDH	L
	8:30	am	Breakfast	D
	12:30	pm	Lunch	D
	5:30	pm	Dinner	D
	7	pm	Finish 12-hour urine collections on all subjects	S,O
			Temperatures on all subjects	O
	9	pm	Lights out	O
	11	pm	T.V. off	O
			Orderly change	O
6	7	am	Finish 12-hour urine collections on all subjects	S,O
			Weights and temperatures on all subjects	O
			Stop urine collections	O
			3 carmine dye capsules for all subjects before breakfast	O
			X-ray densitometry studies on all subjects	M
	7:30	am	Breakfast	D
	8	am	Start modified tilt procedures (without direct intra-arterial blood pressures)	CV
			5 subjects participated in modified tilt procedures: A.C.L., M.G.O., D.C.III., A.C.I., and C.L.B.	
			C.P. returned for modified tilt on 9/9/63 and 9/12/63	
	12:30	pm	Lunch	D
	1	pm	Dismiss all subjects	

INITIAL INTERVIEW, PHYSICAL EXAMINATION AND HISTORY

1. All prospective candidates for the study must be interviewed by a physician.

2. At the time of the interview, the subjects will be acquainted in general terms with the experimental design, with the purposes of the study and the possible risks involved.

3. Each subject shall be selected on the basis of his age, current health, past medical history and psychological fitness.

4. A complete history shall be taken and a complete physical examination shall be done by the physician prior to accepting the subject for the study.

5. The initial evaluation shall include:

   a. Statement of present physical condition
   b. Statement of current psychological fitness
   c. A detailed past medical history
   d. A review of systems
   e. A detailed family history
   f. A detailed statement regarding current habits (eating, smoking, drinking, sleeping, exercise, etc.)

6. The physical examination shall be complete and it shall include an examination of:

   a. General appearance, skin, lymphatic system, head, eyes-ears-nose and throat, neck, spine, chest, (lungs and heart), abdomen, genitalia, extremities, and neurological. Chest X-rays will be taken on each subject.

7. An evaluation of the psychological condition of the subject shall be made by a consultant psychiatrist.

8. An evaluation of the sociological conditions surrounding the subject shall be done by the medical social worker.

9. Each subject shall sign the proper forms and authorizations of release and relinquishing responsibility prior to active participation in the study.

10. Each subject will be admitted to TIRR through routine procedures for the admittance of all patients. Standard admitting forms will be used.

INTAKE AND OUTPUT PROCEDURES

A. INTAKE PROTOCOL

1. All food and liquid intake for each subject shall be recorded in the special source documents.

2. The amount of liquid taken shall be measured exactly. In order to facilitate this measurement, cups measuring eight (8) ounces will be available and when a subject asks for a drink of water, he shall be offered a full cup containing eight (8) ounces. Whatever amount is left after drinking shall be measured exactly in order to compute the amount taken.

3. Each subject shall be asked to eat all food contained on the tray offered to him at each meal. All fluid offered with meals shall be taken in by all subjects.

4. In the event that a subject is unable to ingest all the food or liquid offered on his tray, the amounts left over shall be put back on the tray and sent to the laboratory for measurement and analysis.

B. OUTPUT PROTOCOL

1. Solid and liquid output of each subject shall be collected according to specifications given in the protocols for urine collection and also for fecal collections.

2. If the subject perspires during the period of immobilization, a statement regarding the amount of perspiration shall be included in the source documents of clinical observations.

3. A rating will be made of the degree of perspiration according to the following scale: a. trace, b. fair amount, c. moderate amount, d. large amount, e. profuse.

4. If the subject vomits during the period of study, the attending physician shall be notified immediately. The whole amount of vomitus shall be collected if possible and sent to the laboratory for measurement and analysis.

5. The total amount of blood collected on each subject for blood chemical analysis shall be entered in the intake and output record.

BLOOD COLLECTION PROCEDURES

(Second Period)

CODE

a. Tests
b. Calcium
c. Phosphorus
n. Alkaline phosphatase
o. Blood volume
q. Protein electrophoresis
r. LDH
s. Total protein
t. CBC
Reticulocyte count

Date	Time	Test	Blood to be Drawn	Comments
August				
15	8 am	s,t		
16	8 am	n,q		Draw and inject isotope Draw from opposite arm
19	7:30 am	n a,b,c,o q,r,s Note: n following tilt		Draw and inject isotope Draw from opposite arm
20	7:30 am	n q		Draw and inject isotope Draw from opposite arm
21	7:30 am	n q		Draw and inject isotope Draw from opposite arm
23	7:30 am	n q		Draw and inject isotope Draw from opposite arm
27	7:30 am	n q		Draw and inject isotope Draw from opposite arm

Date	Time	Test	Blood to be Drawn	Comments
September				
1	7:30 am	n		Draw and inject isotope
		C.L.B. Only		Draw from opposite arm
2	7:30 am	a,b,c,o,q,r,s		
		Note: n following tilt		Draw and inject isotope
5	7:30 am	n		Draw and inject isotope
		q		Draw from opposite arm
6		All collections stop		

URINE COLLECTION PROCEDURES
(Second Period)

Date	Time	Test
August		
15	Routine urinalysis on all subjects	2
15	7 am - Start collections for 12-hour pool, 7 am - 7 pm; Repeat the same for the next 12 hours, 7 pm - 7 am the	On 12-hour pools, 4,6,7
15 - 16	morning. The 24-hour pool is considered ended at 7 am on August 16	On 24-hour pool 1
16	7 am - 7 pm	
16 - 17	7 pm - 7 am	As above
17	7 am - 7 pm	
17 - 18	7 pm - 7 am	As above
18	7 am - 7 pm	
18 - 19	7 pm - 7 am	As above
19	Start tilt procedures	
	7 am - Collect to the beginning of tilt and put in bottle for testing as above.	
	NOTE: Each subject must void before being placed on tilt table.	
	Collect from start of tilt to 3 hours after the beginning of tilt procedures. Mark the bottle for this collection with the subject's name and number, the time of the beginning of the tilt procedure, and the time of the end of the 3-hour collection period.	4,6,7

Date	Time	Test
	From the end of the above collection period to 7 pm	4,6,7
19 - 20	7 pm - 7 am	1 (On 24-hour pool)
20	7 am - 7 pm	
20 - 21	7 pm - 7 am	As on August 15, 1963
21	7 am - 7 pm	
21 - 22	7 pm - 7 am	As above
22	7 am - 7 pm	
22 - 23	7 pm - 7 am	As above
23	7 am - 7 pm	
23 - 24	7 pm - 7 am	As above
24	7 am - 7 pm	
24 - 25	7 pm - 7 am	As above
25	7 am - 7 pm	
25 - 26	7 pm - 7 am	As above
26	7 am - 7 pm	
26 - 27	7 pm - 7 am	As above
27	7 am - 7 pm	
27 - 28	7 pm - 7 am	As above
28	7 am - 7 pm	
28 - 29	7 pm - 7 am	As on August 15, 1963
29	7 am - 7 pm	
29 - 30	7 pm - 7 am	As above
30	7 am - 7 pm	
30 - 31	7 pm - 7 am	As above
31	7 am - 7 pm	
31 - Sept. 1	7 pm - 7 am	As above
September		
1	7 am - 7 pm	
1 - 2	7 pm - 7 am	As above

Date	Time	Test
2	Start of tilt procedure	
	7 am - Collect to the beginning of tilt and put in bottle for testing as above.	
	NOTE: Each subject must void before being placed on the tilt table.	
	Collect from the beginning of tilt to 3 hours after the beginning of tilt procedure. Mark the bottle with the subject's name and number, the time of the beginning of the tilt procedure and the time of the end of the collection period.	4,6,7
	From the end of the above collection period to 7 pm.	4,6,7
2 - 3	7 pm - 7 am	1 (on 24-hour pool)
3	7 am - 7 pm	
3 - 4	7 pm - 7 am	As on August 15, 1963
4	7 am - 7 pm	
4 - 5	7 pm - 7 am	As above
5	7 am - 7 pm	
5 - 6	7 pm - 7 am	As above
6	All collections stop	

CODE FOR TESTS

1. Ca, P, N, and Creatinine
2. Routine and microscopic
4. Na, K
6. 17-OH steroids
7. MHMA

FECAL COLLECTION PROCEDURES

(Second Period)

1. Give marker (3 carmine capsules) just before breakfast on Thursday, August 15, 1963

2. Collect every stool in a separate jar from the time the marker first appears. (These jars, pre-weighed will be supplied by the lab.) Each jar will have a number. The source document will be taken on the laboratory by the orderly with the jar for each stool and the source document will bear the same number in the left top corner in red pencil which will correspond to the number on the jar. On the source document the orderly will fill in the: Date, Time.

3. Give marker *again* (3 *carmine capsules*) *just after tilt on Monday*, August 19, 1963 (beginning of immobilization). Continue collecting all feces in separate jars.

4. Give third marker (3 carmine capsules) just before tilt on Monday, September 2, 1963. (End of immobilization)

5. Give fourth marker (3 carmine capsules) just before breakfast on Friday, September 6, 1963.

6. Subjects are all to take feces collecting containers home with them and shall continue to collect feces during this time until the appearance of the carmine. Each jar shall be returned to TIRR as soon as possible. It must be refrigerated if not returned within 4 hours.

PREPARATION FOR TILT TESTING

(With the indicated exceptions the preparation and procedure for tilt testing were the same for the two phases of the immobilization study.)

DATE: July 22, August 5, August 19, and September 2, 1963

Time (Approximate)	Subject No.	Phase I		Phase II	
8 am	1	A.C.L.	70-0-11	A.C.L.	70-0-11
9:30 am	2	T.G.O.	70-0-12	M.G.O.	70-0-13
11 am	3	M.G.O.	70-0-13	D.C. III	70-0-14
1 pm	4	D.C. III	70-0-14	C.L.B.	70-0-16
2:30 pm	5	C.L.B.	70-0-16	C.P.	70-0-17
4 pm	6	C.P.	70-0-17	A.C.I.	70-0-18

NOTE: *Modified tilt procedures were done on August 14,1963, September 6, 1963, and on one subject on September 9,1963,and September 12,1963 (C.P. - 70-0-17). One subject was tilted on September 1,1963, (C.L.B.- 70-0-16, and released because of family emergency.

INSTRUCTIONS

1. One half hour prior to tilt,each subject must have his own electrode harness applied (or checked).

2. An intra-arterial needle must be inserted.

3. An intracath must be inserted in the saphenous vein.

4. The subject must void before being placed on the tilt table.

5. All the urine collected up to 3 hours from the onset of the tilt procedure must be collected and analyzed for MHMA, Na, K.

6. Blood volume measurements will be made before and after tilt unless indicated otherwise on the Master Protocol.

7. Samples of venous blood will be collected at several points during tilt for measurements of corticosteroids.

8. Throughout the passive tilt test the electrocardiogram,pneumogram,carotid pulse,radial pulse,phonocardiogram, intra-arterial pressure, and Korotkoff sounds in the brachial artery during the intermittent inflation of a cuff must be monitored. During the Flack test,the pressure in the airway of the subject must be recorded also.

---

* Without direct intra-arterial blood pressure.

BEDSIDE MONITORING SCHEDULE

(Second Period)

Time	Date	With Exercise	Responsible
	August		
7 pm	15		TOT
7 am			AG
7 pm	17		TOT
9 am		X	AG
7 pm	20		TOT
7 am			AG
7 pm	22		TOT
9 am	26	X	TOT
7 am			AG
7 pm	27		TOT
7 am			AG
7 pm	28		TOT
7 am			AG
7 pm	29		TOT
7 am			Zuniga
7 pm	30		Zuniga
9 am			TOT
7 pm	31	X	Harrison
7 am	September		TOT
7 pm	1		MD on call
7 am	2		AG
7 am	3		AG
7 am	4		AG
7 am	5		AG
	6	All subjects dismissed at 1 pm.	

PROTOCOLS FOR ISOMETRIC EXERCISE

August 19 through September 1, 1963

Nature of this Exercise: Exertion of a thrust force between heels and shoulders on a thrust rack, which lies on the bed surface. Levels of force to be produced by each subject will be determined in advance and assigned individually. Amount of force exerted during each effort will be measured and recorded. The subject will know how much force he is exerting by watching an auxiliary meter. The subject remains in the supine-horizontal position at all times, and only a minor degree (10 to 15 degrees) of knee flexion is permitted.

1. Positioning: Press strongly with shoulders into padded cuffs.
   Press with heels only against footboard, evenly and low on the pressure board.
   Keep lumbar area (low back) flat on table--do not arch back.
   Rotate pelvis to assist keeping back flat; place hands under buttocks.
   Breathe deeply and at regular rate--do not hold your breath at any time.

2. Rounds: Each round of exercise consists of the following continuously timed sequence: five-second effort, with five-second rest interval. Watch the light for the timing and the meter for the control of force level.

   a. Five efforts at assigned level of force (knee flexed)
   b. Two maximum efforts (knee flexed)
   c. Five efforts at assigned level of force (knee flexed)
   d. Five efforts at full extension.

3. Daily schedule of exercise rounds (starting times). One round will take about one hour to complete for all six subjects.

am.	pm.
9:00	1:30
10:00	2:30
11:00	3:30